

HIGHLIGHT set on as ''

? b 411

28jun02 09:06:54 User217743 Session D561.2

\$0.00 0.070 DialUnits File410

\$0.00 Estimated cost File410

\$0.01 TELNET

\$0.01 Estimated cost this search

\$0.01 Estimated total session cost 0.227 DialUnits

File 411:DIALINDEX(R)

DIALINDEX(R)

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*** DIALINDEX search results display in an abbreviated

*** *** format unless you enter the SET DETAIL ON

command. *** ? set files allscience

You have 261 files in your file list.

(To see banners, use SHOW FILES command)

? s extra?neous ()(cys or cysteine or cystine)

Your SELECT statement is:

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Items File

Examined 50 files

Examined 100 files

Examined 150 files

Examined 200 files

Examined 250 files

No files have one or more items; file list includes 261 files.

? s extraneous ()(cys or cysteine or cystine)

Your SELECT statement is:

s extraneous ()(cys or cysteine or cystine)

Items File

Examined 50 files

1 155: MEDLINE(R)_1966-2002/Jun W4

1 156: ToxFile_1966-2002/Mar W4

Examined 100 files

Examined 150 files

2 349: PCT

FULLTEXT_1983-2002/UB=20020627,UT=20020620

1 357: Derwent Biotech Res._1982-2002/Mar W1

Examined 200 files

1 654: US PAT.FULL._1976-2002/Jun 25

Examined 250 files

5 files have one or more items; file list includes 261 files.

? rf

Your last SELECT statement was:

S EXTRANEOUS ()(CYS OR CYSTEINE OR CYSTINE)

Ref Items File

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N1 2 349: PCT

FULLTEXT_1983-2002/UB=20020627,UT=20020620 N2

1 155: MEDLINE(R)_1966-2002/Jun W4

N3 1 156: ToxFile_1966-2002/Mar W4

N4 1 357: Derwent Biotech

Res._1982-2002/Mar W1 N5 1 654: US

PAT.FULL._1976-2002/Jun 25

N6 0 2: INSPEC_1969-2002/Jun W4

N7 0 5: Biosis Previews(R)_1969-2002/Jun W4

N8 0 6: NTIS_1964-2002/Jul W1

N9 0 8: Ei Compendex(R)_1970-2002/Jun W4

N10 0 9: Business &

Industry(R)_Jul/1994-2002/Jun 27 5 files have one or more items; file list includes 261 files.

- Enter P or PAGE for more -

? b n1-n5

28jun02 09:09:16 User217743 Session D561.3

\$5.43 3.101 DialUnits File411

\$5.43 Estimated cost File411

\$0.65 TELNET

\$6.08 Estimated cost this search

\$6.09 Estimated total session cost 3.328 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 349:PCT FULLTEXT

1983-2002/UB=20020627,UT=20020620 (c) 2002

WIPO/Univentio

File 155:MEDLINE(R) 1966-2002/Jun W4

*File 155: Daily alerts are now available. This file has been reloaded. Accession numbers have changed.

File 156:ToxFile 1966-2002/Mar W4

(c) 2002

File 357:Derwent Biotech Res. _1982-2002/Mar W1

(c) 2002 Thomson Derwent & ISI

*File 357: Price changes as of 1/1/02. Please see HELP RATES 357. Derwent announces file enhancements. Please see HELP NEWS 357. File 654:US PAT.FULL. 1976-2002/Jun 25

(c) FORMAT ONLY 2002 THE DIALOG CORP.

*File 654: is redesigned with new search and display features. See HELP NEWS654 for details.

Reassignments current through Dec. 12, 2001.

Set Items Description

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? s extraneous ()(cys or cysteine or cystine)

35545 EXTRANEOUS

37583 CYS

106210 CYSTEINE

16036 CYSTINE

S1 6 EXTRANEOUS ()(CYS OR CYSTEINE OR CYSTINE) ? rd

>>>Duplicate detection is not supported for File 349.

>>>Duplicate detection is not supported for File 654.

>>>Records from unsupported files will be retained in the
RD set.completed examining records
S2 5 RD (unique items)
? t s2/9/all

2/9/1 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00758405 **Image available**
VASCULAR ENDOTHELIAL GROWTH FACTOR DIMERS
DIMERES, FACTEURS DE CROISSANCE DE
L'ENDOTHELIUM VASCULAIRE Patent

Applicant/Assignee:

SCIOS INC, 820 West Maude Avenue, Sunnyvale, CA
94086, US, US (Residence), US (Nationality), (For all
designated states except: US) Patent Applicant/Inventor:

JUE Rodney Alan, 7566 Denison Place, Castro Valley, CA
94552, US, US (Residence), US (Nationality),
(Designated only for: US) SCHELLENBERGER Ute, 914
Moreno Avenue, Palo Alto, CA 94303, US, US

(Residence), DE (Nationality), (Designated only for: US)

STATHIS Peter A, 975 Florence Lane, Apt. F, Menlo
Park, CA 94025, US, US (Residence), US (Nationality),

(Designated only for: US) ADRIAENSSENS Peter
Isadore, 1109 El Monte Avenue, Mountain View, CA 94040,

US, US (Residence), US (Nationality), (Designated only

for: US) ABRAHAM Judith A, 4901 Country Lane, San
Jose, CA 95129, US, US (Residence), US (Nationality),

(Designated only for: US) BALDWIN Patricia Ann, 531
Torwood Lane, Los Altos, CA 94022, US, US

(Residence), US (Nationality), (Designated only for: US)

POLLITT N Stephen, 1037 Campbell Avenue, Los Altos,
CA 94024, US, US (Residence), US (Nationality),

(Designated only for: US) Legal Representative:

ALTMAN Daniel E (agent), Knobbe, Martens, Olson and
Bear, LLP, 16th floor, 620 Newport Center Drive,
Newport Beach, CA 92660, US, Patent and Priority
Information (Country, Number, Date):

Patent: WO 200071716 A2-A3 20001130 (WO

0071716) Application: WO 2000US13636

20000518 (PCT/WO US0013636) Priority Application:

US 99135312 19990520; US 2000177407 20000120

Designated States: AE AG AL AM AT AU AZ BA BB BG

BR BY CA CH CN CR CU CZ CZ (utility model) DE DE

(utility model) DK DK (utility model) DM DZ EE EE

(utility model) ES FI FI (utility model) GB GD GE GH GM

HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT

LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU

SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ

UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC

NL PT SE (OA) BF BJ CF CG CI CM GA GN GW ML MR

NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Main International Patent Class: C12N-015/19

International Patent Class: C07K-014/52; A61K-038/19

Publication Language: English

Filing Language: English

Fulltext Word Count: 25303

English Abstract

This invention concerns novel vascular endothelial
growth factor (VEGF) dimers, compositions containing
such dimers, processes for making such dimers, and
methods for the treatment of various diseases by
administering such dimers or compositions.

French Abstract

L'invention porte sur de nouveaux dimères, facteurs de
croissance de l'endothélium vasculaire (VEGF), sur des
compositions les contenant, sur leurs processus
d'obtention, et sur des méthodes de traitement de
différentes maladies par administration de ces dimères et
de ces compositions.

Legal Status (Type, Date, Text)

Publication 20001130 A2 Without international search
report and to be republished upon receipt

of that report. Examination 20010308 Request for
preliminary examination prior to end of

19th month from priority date

Search Rpt 20010719 Late publication of international
search report Republication 20010719 A3 With
international search report. Detailed Description

84) Designated States (regional): ARIPO patent (GH,
GM, Published.

KE, LS, MVV@ MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian -

Without international search report and to be

republished patent (AM, AZ, BY, KG, KZ, MD, RU, TJ,
TM), European upon receipt of that report.

patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE9
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,

For two-letter codes and other abbreviations, refer to
the "GuidC19 CM, GA, GN, GW, ML, MR, NE, SN, TD,

TG). ance Notes on Codes and Abbreviations" appearing at
the beginning of each regular issue of the PCT Gazette.

Claim

1 A vascular endothelial growth factor (VEGF) dimer
consisting of a first and a second monomer each
comprising at least amino acids 11 to 116 of SEQ ID
NO: 1, or comprising an amino acid sequence having at
least about 90% sequence identity with amino acids 11 to
116 of SEQ ID NO: 1, and retaining a cysteine (Cys) at or
corresponding to position 116 of SEQ ID NO: 1 (Cys-1
16), wherein Cys-116 of each monomer is disulfide-bonded
to an additional *extraneous* *Cys*.

2/3, AB, KWIC/1 (Item 1 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT
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00758405

VASCULAR ENDOTHELIAL GROWTH FACTOR DIMERS
DIMERES, FACTEURS DE CROISSANCE DE
L'ENDOTHELIUM VASCULAIRE Patent

Applicant/Assignee:

SCIOS INC, 820 West Maude Avenue, Sunnyvale, CA
94086, US, US (Residence), US (Nationality), (For all
designated states except: US) Patent Applicant/Inventor:

JUE Rodney Alan, 7566 Denison Place, Castro Valley, CA
94552, US, US (Residence), US (Nationality),

(Designated only for: US) SCHELLENBERGER Ute, 914
Moreno Avenue, Palo Alto, CA 94303, US, US

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(Designated only for: US) ADRIAENSSENS Peter

Isadore, 1109 El Monte Avenue, Mountain View, CA 94040,
US, US (Residence), US (Nationality), (Designated only

for: US) ABRAHAM Judith A, 4901 Country Lane, San
Jose, CA 95129, US, US (Residence), US (Nationality),

(Designated only for: US) BALDWIN Patricia Ann, 531
Torwood Lane, Los Altos, CA 94022, US, US

(Residence), US (Nationality), (Designated only for: US)

POLLITT N Stephen, 1037 Campbell Avenue, Los Altos,
CA 94024, US, US (Residence), US (Nationality),

(Designated only for: US) Legal Representative:

ALTMAN Daniel E (agent), Knobbe, Martens, Olson and
Bear, LLP, 16th floor, 620 Newport Center Drive,
Newport Beach, CA 92660, US, Patent and Priority
Information (Country, Number, Date):

Patent: WO 200071716 A2-A3 20001130 (WO
0071716) Application: WO 2000US13636

20000518 (PCT/WO US0013636) Priority Application:
US 99135312 19990520; US 2000177407 20000120

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY CA CH CN CR CU CZ CZ (utility model) DE DE

(utility model) DK DK (utility model) DM DZ EE EE

(utility model) ES FI FI (utility model) GB GD GE GH GM

HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT

LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU

SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ

UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC

NL PT SE (OA) BF BJ CF CG CI CM GA GN GW ML MR

NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 25303

English Abstract

This invention concerns novel vascular endothelial

growth factor (VEGF) dimers, compositions containing
such dimers, processes for making such dimers, and
methods for the treatment of various diseases by
administering such dimers or compositions.

French Abstract

L'invention porte sur de nouveaux dimeres, facteurs de
croissance de l'endothelium vasculaire (VEGF), sur des
compositions les contenant, sur leurs processus
d'obtention, et sur des methodes de traitement de
differentes maladies par administration de ces dimeres et
de ces compositions.

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... of the Invention

The present invention is based on the recognition that
VEGF₂₁ dimers in which Cys-116 is disulfide bonded to
another, *extraneous* *cysteine* have enhanced
stability while retaining VEGF biological activity. The
invention is further

2

based on the finding that this is true not only for full...

...at a position corresponding to position 116 of SEII ID

NO: 1 (Cys-116), wherein Cys-116 of each monomer is

disulfidebonded to an additional *extraneous*

cysteine (Cys). The additional Cys may be part of a

peptide comprising 2 to 5, preferably 2 to 3 amino acids,

e.g. glutathione. Each monomer...116 of SEG ID NO: 1

(Cys-116), where Cys-116 of each monomer is disulfide

bonded to an additional *extraneous* *Cys* comprising

the steps of.

(a) providing transformed bacterial host cells comprising

a species of exogenously added DNA encoding a

polypeptide of SEG ID NO: 1... 25:3389-3402 (1997).

The parameters are set to default values, with the

exception of Penalty for mismatch, which is set to - 1.

The terms "*extraneous* *cysteine*" or "additional

cysteine" or "additional *extraneous* *cysteine*" in the

context of the present invention are used to refer to a

cysteine that is not directly encoded by a nucleic acid

sequence encoding...

...at least one VEGF monomer, the cysteine at a position

corresponding to position 116 in the native human

VEGF₁₂, molecule is disulfide-bonded to an *extraneous*

cysteine will also be referred to as a "mixed disulfide"

structure. In some instances, the *extraneous*

cysteine may be part of a peptide, such as a glutathione

molecule. 15 The term "unpaired" in reference to a

cysteine at a position corresponding...DNA technology,

hVEGF₂₁ dimers in which at least one, and preferably both, cysteines at positions 116 of the monomers, are disulfide-bonded to an *extraneous* *cysteine*.

We have additionally found that the stability and biological activity of recombinant hVEGF₁₂ dimers are not compromised by amino acid deletions, substitutions or insertions at...product. Expression in mammalian cells may be performed to produce a dimer in which Cys-116 in each monomer is predominantly attached to an *extraneous* *cysteine* via a disulfide bond. In a smaller fraction of the dimers produced, cysteines-116 in the two monomers are coupled by an...

...6, and produce at least about 15

% mixed disulfide, in which Cys-116 in each monomer is disulfide-bonded to an *extraneous* *cysteine*, which may be part of a peptide molecule, e.g. glutathione.

Typically, the cDNA encoding the monomeric chains of the desired VEGF₂ dimer is...linked sugar was found to have either one or two sialic acid moieties. Finally, the LC-MS data suggested that in some cases, two extra (*extraneous*) *cysteine* molecules had become bonded to the VEGF dimer (i.e., the molecular weight was increased by 240 atomic mass units [amu], consistent with the addition...

...addition, this mass clearly distinguishes between a number of different states for Cys-116. If Cys-116 has become disulfidebonded to an additional *extraneous* *cysteine* molecule, then the mass of the C-terminal Glu-C peptide will represent residues 115 - 120, plus 120 amu (for a total mass of...dimers generated as described in Section B above, the Arg at position 121 was lost, and Cys-116 was sometimes disulfide bonded to an *extraneous* *cysteine* 115 and sometimes bonded to the other Cys-116 in the dimer.

Example 2

Production of hVEGF₁₂ in f. coli host cells
A...

Claim

... corresponding to position 116 of SEQ ID NO: 1 (Cys-116), wherein Cys-116 of each monomer is disulfide-bonded to an additional *extraneous* *Cys*.

2 The VEGF dimer of claim 1 wherein in at least one of said first and second monomers said additional Cys is part of a...

...at or corresponding to position 116 of SEQ ID NO: 1 (Cys-116), wherein Cys-116 of each monomer is disulfide bonded to an additional *extraneous* *Cys*, in

admixture with a pharmaceutically acceptable vehicle.
40

The composition of claim 14 wherein in at least one of said first and second monomers said...

...116 of SEQ ID NO: 1 (Cys-116), and Cys-116 of each monomer is disulfide-bonded to an additional *extraneous* *Cys*; (b) a dimer in which each monomer comprises amino acids 11 to 116 of SEQ ID NO: 1, or comprises an amino...116 of SEQ ID NO: 1 (Cys-116), and Cys-116 of each

monomer is disulfide bonded to an additional *extraneous* *Cys*; (b) a dimer in which each monomer comprises amino acids 11 to 116 of SEQ ID NO: 1, or comprises an amino...a position corresponding to position 116 of SEQ ID NO: 1 (Cys-116), where Cys-116 of each monomer is disulfide bonded to an additional *extraneous* *Cys*, comprising the steps of: (a) providing transformed bacterial host cells comprising a species of exogenously added DNA encoding I O a polypeptide of SEQ ID...

2/3, AB, KWIC/2 (Item 2 from file: 349)

DIALOG(R) File 349: PCT FULLTEXT

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00314138

HEPATITIS G VIRUS AND MOLECULAR CLONING
THEREOF

VIRUS DE L'HEPATITE G ET SON CLONAGE
MOLECULAIRE

Patent Applicant/Assignee:

GENELABS TECHNOLOGIES INC,

Inventor(s):

KIM Jungsuh P,
FRY Kirk E,
YOUNG Lavonne Marie,
LINNEN Jeffrey M,
WAGES John,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9532291 A2 19951130

Application: WO 95US6169 19950519 (PCT/WO

US9506169) Priority Application: US 94246985

19940520; US 94285543 19940803; US 94285558

19940803; US 94329729 19941026; US 94344271

19941123; US 94357509 19941216; US 95389886

19950215

Designated States: AM AT AU BB BG BR BY CA CH CN
CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR
LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD
SE SI SK TJ TT UA UZ VN KE MW SD SZ UG AT BE
CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ
CF CG CI CM GA GN ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 102890

English Abstract

Polypeptide antigens are disclosed which are immunoreactive with sera from individuals having a non-A, non-B, non-C, non-D, non-E Hepatitis, herein designated Hepatitis G virus (HGV). Corresponding genomic-fragment clones containing polynucleotides encoding the open reading frame sequences for the antigenic polypeptides are taught. The antigens are useful in diagnostic methods for detecting the presence of HGV in test subjects. The antigens are also useful in vaccine and antibody preparations. In addition, the entire coding sequences of two HGV isolates are disclosed. Methods are presented for nucleic acid-based detection of HGV in samples and also methods for the isolation of further genomic sequences corresponding to HGV.

French Abstract

L'invention concerne des antigenes polypeptidiques qui sont immunoreactifs avec des serums provenant de personnes ayant une hepatite non A, non B, non C, non D, non E, designee ici virus de l'hepatite G (HGV). Des clones de fragments genomiques correspondants contenant des polynucleotides codant les sequences de structures a lecture directe provenant de polypeptides antigeniques sont egalement concernes. Les antigenes sont utiles dans des procedes diagnostics pour la detection de la presence du HGV dans des sujets soumis aux tests. Les antigenes sont egalement utiles dans des preparations de vaccins et d'anticorps. De plus, toutes les sequences de codage des deux isolats HGV sont decrites. L'invention decrit egalement la detection basee sur l'acide nucleique de HGV dans des echantillons, ainsi que des procedes permettant d'isoler d'autres sequences genomiques correspondant a HGV.

Fulltext Availability:

Detailed Description

Detailed Description

... PEP7/NS4A 18 5275/5328

PEP8/NS4B 16 6097/6144

PEP9/NS5A 16 7033/7080

PEP10/NS5B 18 7783/7836

The NS3 peptide has an *extraneous* *Cysteine* on the C terminal end that is not in the HGV-PNF 2161 variant polypeptide sequence; the actual sequence was a Q.

The peptides were...

2/3,AB,KWIC/3 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

06100868 89193277 PMID: 3071326

Production of recombinant human colony stimulating

factors in yeast. Gillis S; Urdal D L; Clevenger W; Klinke R; Sassenfeld H; Price V; Cosman D

Department of Molecular Biology, Immunex Corporation, Seattle, Washington 98101.

Behring Institute Mitteilungen (GERMANY, WEST) Aug 1988, (83) p1-7, ISSN 0301-0457 Journal Code: 0367532

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Efficient yeast expression and purification systems for production of recombinant human GM-CSF, IL-3 and G-CSF have been established. Though yeast-derived production of recombinant CSFs (through the use of secretion based system) allows for generation of native molecules which can then be readily separated from fermentation broth, in many instances, natural cDNAs have had to be altered to allow for efficient expression, as well as production of a less heterogeneous product. In the case of CSFs described herein, beneficial mutations (made through site-directed mutagenesis) have included elimination of potential N-linked glycosylation sites, removal of KexII protease recognition sites (notably alterations in dibasic sequences) and elimination of *extraneous* *cysteine* residues which might complicate isolation of a homogeneous product due to intermolecular disulfide bonding.

... directed mutagenesis) have included elimination of potential N-linked glycosylation sites, removal of KexII protease recognition sites (notably alterations in dibasic sequences) and elimination of *extraneous* *cysteine* residues which might complicate isolation of a homogeneous product due to intermolecular disulfide bonding.

2/3,AB,KWIC/4 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0264133 DBA Accession No.: 2001-03887 PATENT

Vascular endothelial growth factor dimer, useful for treating essential hypertension, polycystic kidney diseases, microvascular angiopathy and coronary artery disease, comprising two monomeric subunits - vascular endothelial cell growth factor dimer for use in therapy

AUTHOR: Jue R A; Schellenberger U; Stathis P A; Adriaenssens P I; Abraham J A; Baldwin P A; Pollitt N S

CORPORATE SOURCE: Sunnyvale, CA, USA.

PATENT ASSIGNEE: Scios 2000

PATENT NUMBER: WO 200071716 PATENT DATE:

20001130 WPI ACCESSION NO.: 2001-041064 (2005)

PRIORITY APPLIC. NO.: US 177407 APPLIC. DATE:
20000120
NATIONAL APPLIC. NO.: WO 2000US13636 APPLIC.
DATE: 20000518 LANGUAGE: English
ABSTRACT: A vascular endothelial cell growth factor
(VEGF) dimer (I) comprising a 1st and 2nd monomer,
each comprising at least amino acids 11-116 of a defined
147 amino acid protein sequence (S1) (disclosed) or a
sequence having over 90% sequence identity to (S1) and
retaining a cysteine at or corresponding to position 116,
which is disulfide-bonded to an extra *extraneous*
Cys, is claimed. Also claimed are: a composition of
(I); a composition comprising more than 2 VEGF dimers,
each formed by a 1st and 2nd monomer selected from a
dimer in which each monomer is disulfide-bound to
an *extraneous* *Cys*, a dimer in which the 2
monomers are connected with an interchain disulfide
bond, or a dimer in which one or both of its monomers
is unpaired, provided that each monomer comprises
(S1) or a sequence with over 90% identity to (S1)
and are independently glycosylated or unglycosylated;
providing the composition of matter; producing a VEGF
dimer; and blocking removal of one or more amino acids
from the mature N-terminus of a proein during
production in a bacterial host cell. (61pp)

...ABSTRACT: sequence having over 90% sequence
identity to (S1) and retaining a cysteine at or
corresponding to position 116, which is
disulfide-bonded to an extra *extraneous* *Cys*, is
claimed. Also claimed are: a composition of (I); a
composition comprising more than 2 VEGF dimers, each
formed by a 1st and 2nd monomer selected from a
dimer in which each monomer is disulfide-bound to an
extraneous *Cys*, a dimer in which the 2
monomers are connected with an interchain disulfide
bond, or a dimer in which one or both of its
monomers...

2/3,AB,KWIC/5 (Item 1 from file: 654)
DIALOG(R)File 654:US PAT.FULL.
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reserv.

2114430
Derwent Accession: 1976-38160X
Utility
REASSIGNED
C/ Keratin modifying agents and method of beneficially
modifying filamentous keratin materials; OXIDATION
Inventor: Karjala, Sulo A., Chicago, IL
Assignee: Wilson Foods Corporation (02), Oklahoma City,
OK WILSON FOODS CORP (Code: 00975)
Examiner: Friedman, Stanley J. (Art Unit: 125)
Law Firm: Dressler, Goldsmith, Clement, Gordon & Shore,

Ltd.

Publication Number	Kind	Date	Application Number	Filing Date	
US 4041150	A	19770809	US 71147623	19710527	Main Patent
Priority			US 71147623	19710527	

Abstract:

The invention relates to materials which are
beneficiating agent derivatives for bonding a
beneficiating agent to filamentous keratins such as hair
and wool and effect modification of the filamentous
keratins by being chemically coupled thereto so as to
become an integral part thereof. The materials for
improving the properties of filamentous keratins
comprise polypeptides having intact disulfide linkages and
having an agent molecularly joined thereto through a bond
independent of the disulfide linkages to form a
polypeptide derivative. Such a derivative is chemically
bonded to the filamentous keratins by a two-step
process wherein disulfide linkages of both the derivatives
and the filamentous keratins are split by the action of a
reducing agent and disulfide linkages are then reformed
by action of an oxidizing agent whereby at least some of
the sulfhydryl groups formed by the action on the
derivatives of the reducing agent are bonded to
sulfhydryl groups of the filamentous keratins.
Document type: C REASSIGNED

Description of the Invention:

...somewhat whiter color than the original material, but
the heated swatches showed some shrinkage after five
washings of each swatch in boiling alcohol to remove
extraneous *cystine* palmitate... ? b 411

28jun02 09:12:46 User217743 Session D561.4

\$25.26 5.317 DialUnits File349

\$14.70 2 Type(s) in Format 9

\$10.90 2 Type(s) in Format 5 (UDF)

\$25.60 4 Types

\$50.86 Estimated cost File349

\$0.06 0.019 DialUnits File155

\$0.21 1 Type(s) in Format 4 (UDF)

\$0.21 1 Types

\$0.27 Estimated cost File155

\$0.05 0.019 DialUnits File156

\$0.05 Estimated cost File156

\$0.23 0.014 DialUnits File357

\$2.70 1 Type(s) in Format 5 (UDF)

\$2.70 1 Types

\$2.93 Estimated cost File357

\$0.30 0.050 DialUnits File654

\$2.90 1 Type(s) in Format 5 (UDF)

\$2.90 1 Types

\$3.20 Estimated cost File654

OneSearch, 5 files, 5.419 DialUnits FileOS

\$0.86 TELNET

\$58.17 Estimated cost this search
 \$64.26 Estimated total session cost 8.747 DialUnits
 File 411:DIALINDEX(R)

DIALINDEX(R)

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*** DIALINDEX search results display in an abbreviated
 *** *** format unless you enter the SET DETAIL ON
 command. *** ? set files allscience
 You have 261 files in your file list.
 (To see banners, use SHOW FILES command)
 ? s (free or extra)()(cys or cysteine)

Your SELECT statement is:

s (free or extra)()(cys or cysteine)

Items	File
2	2: INSPEC_1969-2002/Jun W4
357	5: Biosis Previews(R)_1969-2002/Jun W4
3	6: NTIS_1964-2002/Jul W1
1	8: Ei Compendex(R)_1970-2002/Jun W4
20	10: AGRICOLA_70-2002/Jun
3	16: Gale Group PROMT(R)_1990-2002/Jun
27	1 18: Gale Group F&S
	Index(R)_1988-2002/Jun 27 1 19:
	Chem.Industry Notes_1974-2002/ISS 200226
1	28: Oceanic Abst._1964-2002/Jun
	271 34: SciSearch(R) Cited Ref
	Sci_1990-2002/Jun W5 27 35: Dissertation
	Abs Online_1861-2002/May 3 40:
	Enviroline(R)_1975-2002/May
	10 44: Aquatic Sci&Fish Abs_1978-2002/Jul
20	47: Gale Group Magazine
	DB(TM)_1959-2002/Jun 28 43 50: CAB
	Abstracts_1972-2002/May
22	51: Food Sci.&Tech.Abs_1969-2002/Jun
W2	5 53: FOODLINE(R): Food Science &
	Technology_1972-2002/Jun 26
1	62: SPIN(R)_1975-2002/Jun W1
1	65: Inside Conferences_1993-2002/Jun W4
1	70: SEDBASE_1996/Jan Q1
157	71: ELSEVIER BIOBASE_1994-2002/Jun
W4	
	273 73: EMBASE_1974-2002/Jun W3
1	74: Int.Pharm.Abs._1970-2002/May
116	76: Life Sciences
	Collection_1982-2002/Jun 1 77: Conference
	Papers Index_1973-2002/May Examined 50 files
24	94: JICST-EPlus_1985-2002/May W1
25	98: General Sci
	Abs/Full-Text_1984-2002/May 9 103: Energy
	SciTec_1974-2002/Jun B2
2	109: Nuclear Sci. Abs._1948-1976
1	119: Textile Technol.Dig._1978-2002/Jun

1	129: PHIND(Archival)_1980-2002/Jun W4
3	143: Biol. & Agric. Index_1983-2002/May
75	144: Pascal_1973-2002/Jun W4
1	148: Gale Group Trade & Industry
	DB_1976-2002/Jun 28 22 149: TGG
	Health&Wellness DB(SM)_1976-2002/Jun W3
365	155: MEDLINE(R)_1966-2002/Jun W4
81	156: ToxFile_1966-2002/Mar W4
1	160: Gale Group PROMT(R)_1972-1989
3	161: Occ.Saf.& Hth._1973-1998/Q3
3	172: EMBASE Alert_2002/Jun W4
2	180: Federal Register_1985-2002/Jun 27
2	185: Zoological Record
	Online(R)_1978-2002/Jun Examined 100 files
2	203: AGRIS_1974-2002/Mar
8	266: FEDRIP_2002/Apr
12	285: BioBusiness(R)_1985-1998/Aug W1
2	292: GEOBASE(TM)_1980-2002/Jun
10	305: Analytical Abstracts_1980-2002/Jun
W3	6 315: ChemEng & Biotec
	Abs_1970-2001/Dec 2 323: RAPRA Rubber &
	Plastics_1972-2002/Aug Examined 150 files
	19 340: CLAIMS(R)/US Patent_1950-02/Jun
25	5 342: Derwent Patents Citation
	Indx_1978-01/200176C 3 345: Inpadoc/Fam.&
	Legal Stat_1968-2002/UD=200224 1 347:
	JAPIO_Oct 1976-2002/Feb(Updated 020604)
113	348: EUROPEAN PATENTS_1978-2002/Jun W03
364	349: PCT
	FULLTEXT_1983-2002/UB=20020627,UT=20020620
32	357: Derwent Biotech Res._1982-2002/Mar
W1	6 358: Current BioTech
	Abs_1983-2001/Oct
4	370: Science_1996-1999/Jul W3
27	399: CA SEARCH(R)_1967-2002/UD=13626
2	434: SciSearch(R) Cited Ref
	Sci_1974-1989/Dec 273 440: Current Contents
	Search(R)_1990-2002/Jun 28 2 442: AMA
	Journals_1982-2002/Jun B2
2	452: Drug Data Report_1992-2002/May
2	457: The Lancet_1986-2000/Oct W1
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17	484: Periodical Abs
	Plustext_1986-2002/Jun W4 1 621: Gale
	Group New Prod.Annou.(R)_1985-2002/Jun 27 1
	624: McGraw-Hill Publications_1985-2002/Jun 27
5	636: Gale Group Newsletter
	DB(TM)_1987-2002/Jun 27 1 652: US Patents
	Fulltext_1971-1975
413	654: US PAT.FULL._1976-2002/Jun 25
	Examined 250 files
1	764: BCC Market Research_1989-2002/Jun

71 files have one or more items; file list includes 261 files.
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Your last SELECT statement was:
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N2	365	155: MEDLINE(R)_1966-2002/Jun W4
N3	364	349: PCT
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	357	5: Biosis Previews(R)_1969-2002/Jun W4 N5
	273	73: EMBASE_1974-2002/Jun W3
N6	273	440: Current Contents
Search(R)_1990-2002/Jun 28 N7 271 34:		
SciSearch(R) Cited Ref Sci_1990-2002/Jun W5 N8		
157	71:	ELSEVIER BIOBASE_1994-2002/Jun W4
N9	116	76: Life Sciences
Collection_1982-2002/Jun N10 113 348:		
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have one or more items; file list includes 261 files.		
- Enter P or PAGE for more -		

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N2	365	155: MEDLINE(R)_1966-2002/Jun W4
N3	364	349: PCT
FULLTEXT_1983-2002/UB=20020627,UT=20020620 N4		
	357	5: Biosis Previews(R)_1969-2002/Jun W4 N5
	273	73: EMBASE_1974-2002/Jun W3
N6	273	440: Current Contents
Search(R)_1990-2002/Jun 28 N7 271 34:		
SciSearch(R) Cited Ref Sci_1990-2002/Jun W5 N8		
157	71:	ELSEVIER BIOBASE_1994-2002/Jun W4
N9	116	76: Life Sciences
Collection_1982-2002/Jun N10 113 348:		
EUROPEAN PATENTS_1978-2002/Jun W03 71 files		
have one or more items; file list includes 261 files.		
- Enter P or PAGE for more -		

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Your last SELECT statement was:
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N11	81	156: ToxFile_1966-2002/Mar W4
N12	75	144: Pascal_1973-2002/Jun W4
N13	43	50: CAB Abstracts_1972-2002/May
N14	32	357: Derwent Biotech
Res_1982-2002/Mar W1 N15 27 35:		
Dissertation Abs Online_1861-2002/May N16 27		
399: CA SEARCH(R)_1967-2002/UD=13626		
N17	25	98: General Sci
Abs/Full-Text_1984-2002/May N18 24 94:		

JICST-EPlus_1985-2002/May W1
N19 22 51: Food Sci.&Tech.Abs_1969-2002/Jun
W2 N20 22 149: TGG Health&Wellness
DB(SM)_1976-2002/Jun W3 71 files have one or more
items; file list includes 261 files.

- Enter P or PAGE for more -

? b n2-n4, n10, n15

28jun02 09:15:42 User217743 Session D561.5

\$5.44 3.110 DialUnits File411

\$5.44 Estimated cost File411

\$0.65 TELNET

\$6.09 Estimated cost this search

\$70.35 Estimated total session cost 11.856 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1966-2002/Jun W4

*File 155: Daily alerts are now available. This file has
been reloaded. Accession numbers have changed.

File 349:PCT FULLTEXT

1983-2002/UB=20020627,UT=20020620 (c) 2002

WIPO/Univentio

File 5:Biosis Previews(R) 1969-2002/Jun W4

(c) 2002 BIOSIS

File 348:EUROPEAN PATENTS 1978-2002/Jun W03

(c) 2002 European Patent Office

File 35:Dissertation Abs Online 1861-2002/May

(c) 2002 ProQuest Info&Learning

Set Items Description

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disulphide) 1223481 FREE

141487 EXTRA

40410 CYS

125381 CYSTEINE

1226 (FREE OR EXTRA)(W)(CYS OR CYSTEINE)

72618 DISULFIDE

11101 DISULPHIDE

S1 657 (FREE OR EXTRA)()(CYS OR CYSTEINE)

AND (DISULFIDE OR DISULPHIDE)

? s (free or extra)()(cys or cysteine) and (disulfide or
disulphide)()bond? 1223481 FREE

141487 EXTRA

40410 CYS

125381 CYSTEINE

1226 (FREE OR EXTRA)(W)(CYS OR CYSTEINE)

72618 DISULFIDE

11101 DISULPHIDE

415991 BOND?

30877 (DISULFIDE OR DISULPHIDE)(W)BOND?

S2 465 (FREE OR EXTRA)()(CYS OR CYSTEINE)

AND (DISULFIDE OR DISULPHIDE)()BOND?

? rd

>>>Duplicate detection is not supported for File 349.

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>>>Records from unsupported files will be retained in the

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...examined 50 records (100)

...examined 50 records (150)

...examined 50 records (200)

...examined 50 records (250)

...examined 50 records (300)

...examined 50 records (350)

...examined 50 records (400)

...examined 50 records (450)

...completed examining records

S3 403 RD (unique items)

? s s3 and vegf

403 S3

15681 VEGF

S4 31 S3 AND VEGF

? t s4/3,ab/all

4/3,AB/1 (Item 1 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00892941

71 HUMAN SECRETED PROTEINS

71 PROTEINES HUMAINES SECRETEES

Patent Applicant/Assignee:

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HOOVER Kenley K (et al) (agent), Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200226931 A2 20020404 (WO

0226931) Application: WO 2001US29871

20010924 (PCT/WO US0129871) Priority Application:

US 2000234925 20000925; WO 2001US911 20010112

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 355828

English Abstract

The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

French Abstract

La presente invention concerne de nouvelles proteines humaines secretees et des acides nucleiques isolés contenant les regions codantes de ces genes codant pour ces proteines. L'invention concerne également des vecteurs, des cellules hotes, des anticorps et des methodes de recombinaison destinees a la production de proteines humaines secretees. L'invention concerne également des methodes diagnostiques et therapeutiques destinees au diagnostic et au traitement de maladies, de troubles et/ou d'etats associes a ces nouvelles proteines humaines secretees.

4/3,AB/2 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00892899

IGF RECEPTOR ANTAGONISTS
ANTAGONISTES DU RECEPTEUR D'IGF

Patent Applicant/Assignee:

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(For all designated states except: US) Patent

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200226781 A2 20020404 (WO
0226781) Application: WO 2001US30289
20010926 (PCT/WO US0130289) Priority Application:
US 2000235353 20000926; US 2001278540 20010323
Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE
ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW
MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ
TM TR TT TZ UA UG US UZ VN YU ZA ZW (EP) AT BE
CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN
TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 166285

English Abstract

The invention provides novel compounds which bind to the high affinity receptor for immunoglobulin E (IgE) designated FcepsilonRI and methods for identifying and preparing such compounds. In particular aspects, the invention provides to the treatment of disorders mediated by IgE utilizing the novel compounds of the invention. The invention also provides compositions, such as pharmaceutical compositions, comprising the novel

compounds, as well as for their use in research, diagnostic, therapeutic, and prophylactic methods.

French Abstract

L'invention concerne de nouveaux composés se liant à un récepteur de haute affinité pour l'immunoglobuline E (IgE), désigné par FcepsilonRI, ainsi que des procédés d'identification et de préparation de tels composés. Sous des aspects particuliers, l'invention concerne le traitement de troubles occasionnés par IgE, traitement utilisant les nouveaux composés de l'invention. L'invention concerne en outre des compositions, telles que des compositions pharmaceutiques, renfermant les nouveaux composés, ainsi que leur utilisation en recherche et dans des méthodes de diagnostic, thérapeutiques et prophylactiques.

4/3,AB/3 (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00855804

METHODS FOR REFOLDING PROTEINS
CONTAINING *FREE* *CYSTEINE* RESIDUES
PROCEDE DE REPLIEMENT DE PROTEINES
RENFERMANT DES RESIDUS DE CYSTEINE LIBRE

Patent Applicant/Assignee:

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Patent Applicant/Inventor:

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(Designated only for: US) COX George N, 678 West
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80202-5141, US,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200187925 A2 20011122 (WO
0187925) Application: WO 2001US16088
20010516 (PCT/WO US0116088) Priority Application:
US 2000204617 20000516

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI
GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
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MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 46084

English Abstract

The present invention relates to novel methods for making and refolding insoluble or aggregated proteins having free cysteines in which a host cell expressing the protein is exposed to a cysteine blocking agent. The soluble, refolded proteins produced by the novel methods can then be modified to increase their effectiveness. Such modifications include attaching a PEG moiety to form PEGylated proteins.

French Abstract

La presente invention concerne des nouveaux procedes de preparation et de repliement de proteines insolubles ou agregees renfermant des cysteines libres, une cellule hote exprimant la proteine etant exposee a un agent bloquant la cysteine. On peut modifier ensuite les proteines solubles et repliees obtenues au moyen des nouveaux procedes, afin d'accroitre leur efficacite. Ces modifications consistent a fixer un groupe PEG en vue de former des proteines PEGylees.

4/3,AB/4 (Item 4 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00843775

COMPOUNDS AND METHODS FOR MODULATING
ENDOTHELIAL CELL ADHESION COMPOSES ET
PROCEDES DE MODULATION DE L'ADHESION DES
CELLULES ENDOTHELIALES Patent Applicant/Assignee:

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Priority Information (Country, Number, Date):

Patent: WO 200177146 A2 20011018 (WO

0177146) Application: WO 2001US11669

20010409 (PCT/WO US0111669) Priority Application:

US 2000544782 20000407

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX
MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 23919

English Abstract

Cyclic peptides comprising a cadherin cell adhesion
recognition sequence HAV, and compositions comprising
such cyclic peptides, are provided. Methods for using
such peptides for modulating cadherin-mediated
endothelial cell adhesion in a variety of contexts are also
provided.

French Abstract

L'invention concerne des peptides cycliques comprenant
une sequence HAV de reconnaissance de l'adhesion
cellulaire de la cadherine et des compositions
renfermant de tels peptides cycliques. L'invention
concerne egalement des procedes d'utilisation de ces
peptides permettant de moduler l'adhesion des cellules
endotheliales dans une variete de contextes.

4/3,AB/5 (Item 5 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00840424

NON-HUMAN TRANSGENIC ANIMALS EXPRESSING
PLATELET-DERIVED GROWTH FACTOR C (PDGF-C)
AND USES THEREOF

ANIMAUX TRANSGENIQUES NON HUMAINS
EXPRIMANT UN FACTEUR DE CROISSANCE C
DERIVE DE PLAQUETTES (PDGF-C) ET UTILISATIONS
Patent Applicant/Assignee:

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Legal Representative:

EVANS Joseph D (agent), Evenson, McKeown, Edwards &
Lenahan, P.L.L.C., 1200 G Street, N.W., Suite 700,
Washington, DC 20005, US, Patent and Priority
Information (Country, Number, Date):

Patent: WO 200172132 A1 20011004 (WO
0172132) Application: WO 2001US9855 20010328
(PCT/WO US0109855) Priority Application: US
2000192507 20000328

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI
GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
TZ UA UG UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 8591

English Abstract

Non-human transgenic animals overexpressing PDGF-C
and cells thereof have been created. The transgenic
animals contain a nucleotide sequence that encodes for
platelet derived growth factor C (PDGF-C) or an analog
thereof. These animals are useful for studying disease
states characterized by overexpression of PDGF-C, as
well as useful for evaluating therapies intended to treat
such diseases.

French Abstract

Cette invention concerne la creation d'animaux
transgeniques non humains qui surexpriment le facteur
de croissance PDGF-C et des cellules de ce facteur. Ces
animaux transgeniques renferment une sequence
nucleotidique qui code pour la plaquette derivee du
facteur de croissance C (PDGF-C) ou d'un analogue. Ces
animaux sont utiles pour l'etude de cas pathologiques
caracterises par une surexpression de PDGF-C, ainsi que
pour l'evaluation de therapies pour de telles maladies.

4/3,AB/6 (Item 6 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00834529

HUMAN GENES AND GENE EXPRESSION PRODUCTS
NOUVEAUX GENES HUMAINS ET LEURS PRODUITS
D'EXPRESSION

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BLACKBURN Robert P (agent), Chiron Corporation, P.O. Box 8097, Emeryville, CA 94662-8097, US, Patent and Priority Information (Country, Number, Date): Patent: WO 200166753 A2 20010913 (WO 0166753) Application: WO 2001US7787 20010309 (PCT/WO US0107787) Priority Application: US 2000188609 20000309

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

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Fulltext Word Count: 182260

English Abstract

This invention relates to novel human polynucleotides and variants thereof, their encoded polypeptides and variants thereof, to genes corresponding to these polynucleotides and to proteins expressed by the genes. The invention also relates to diagnostic and therapeutic agents employing such novel human polynucleotides, their corresponding genes or gene products, e.g., these genes and proteins, including probes, antisense constructs, and antibodies.

French Abstract

L'invention porte sur de nouveaux polynucleotides humains et leurs variantes, sur les polypeptides codes par eux et leurs variantes, sur les genes correspondant a ces polynucleotides, et sur des proteines exprimees par ces genes. L'invention porte egalement sur des agents diagnostiques et therapeutiques utilisant lesdits nouveaux polynucleotides humains et les genes et produits geniques correspondants, ces genes et proteines comportant des sondes, des produits d'assemblage et des anticorps.

4/3,AB/7 (Item 7 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00824932

NUCLEIC ACID MOLECULES ENCODING TRANSMEMBRANE SERINE PROTEASES, THE ENCODED PROTEINS AND METHODS BASED THEREON

MOLECULES D'ACIDES NUCLEIQUES CODANT POUR DES PROTEASES A SERINE TRANSMEMBRANAIRES, PROTEINES CODEES ET PROCEDES ASSOCIES Patent Applicant/Assignee:

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SEIDMAN Stephanie L (et al) (agent), Heller Ehrman White & McAuliffe LLP, Suite 700, 4250 Executive Square, La Jolla, CA 92037, US, Patent and Priority Information (Country, Number, Date):

Patent: WO 200157194 A2-A3 20010809 (WO 0157194) Application: WO 2001US3471 20010202 (PCT/WO US0103471) Priority Application: US 2000179982 20000203; US 2000183542 20000218; US 2000213124 20000622; US 2000220970 20000726; US 2000657986 20000908; US 2000234840 20000922 Parent Application/Grant:

Related by Continuation to: US 2000179982 20000203 (CIP); US 2000183542 20000218 (CIP); US 2000213124 20000622 (CIP); US 2000220970 20000726 (CIP); US 2000657986 20000908 (CIP); US

2000234840 20000922 (CIP) Designated States: AE AG AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 65490

English Abstract

Provided herein are polypeptides that include the protease domain of a type II transmembrane serine protease (MTSP) as a single chain. Methods using the polypeptides to identify compounds that modulate the protease activity of an MTSP are provided. Also provided are MTSPs designated MTSP3 and MTSP4 and a form of an MTSP designated MTSP6.

French Abstract

L'invention concerne des polypeptides comportant un domaine de protease du type de protease a serine transmembranaire de type II (MTSP) sous forme d'une chaine unique. Elle concerne aussi des procedes utilisant ces polypeptides afin d'identifier des composees qui modulent l'activite protease d'une MTSP. Elle concerne encore des MTSP de designation MTSP3 et MTSP4 ainsi qu'une forme de MTSP de designation MTSP6.

4/3,AB/8 (Item 8 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00823009

NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS

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HOOVER Kenley K (et al) (agent), Human Genome Sciences, Inc., 9410 Key West Avenue, 4/3,AB/10 (Item 10 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00804355

VARIANTS OF ALTERNATIVE SPLICING
VARIANTS D'EPISSAGE ALTERNATIF

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Patent: WO 200136632 A2-A3 20010525 (WO 0136632) Application: WO 2000IL766 20001117 (PCT/WO IL0000766) Priority Application: IL 132978 19991117; IL 133455 19991210 Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 111764

English Abstract

The present invention concerns novel variants, amino acid and nucleic acid sequences obtained by alternative splicing of known sequences, expression vectors and host cells containing the variants' nucleic acid sequence, and antibodies reactive with the variants' products. The invention also concerns pharmaceutical compositions containing any of the above as well as methods of detection. A preferred example is the angiotensin converting enzyme (ACE) variant.

French Abstract

L'invention concerne de nouveaux variants, de nouveaux acides amines et de nouvelles sequences obtenues par un epissage alternatif de sequences connues, de vecteurs d'expression et de cellules hotes contenant la sequence d'acide nucleique des variants, et des anticorps reagissant avec les produits des variants. L'invention concerne egalement des compositions pharmaceutiques contenant un ou plusieurs elements precites, ainsi que des procedes de detection. Un exemple prefere est le variant de l'enzyme de conversion de l'angiotensine (ACE).

4/3,AB/11 (Item 11 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT
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00802456

6 HUMAN SECRETED PROTEINS
6 PROTEINES HUMAINES SECRETEES

Patent Applicant/Assignee:

HUMAN GENOME SCIENCES INC, 9410 Key West Avenue, Rockville, MD 20850, US, US (Residence), US (Nationality), (For all designated states except: US) invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

French Abstract

L'invention concerne de nouvelles proteines humaines secretees et des acides nucleiques isoles contenant les regions de codage des genes codant pour lesdites proteines. L'invention concerne egalement des vecteurs, des cellules hotes, des anticorps, et des techniques de recombinaison permettant de produire les proteines humaines secretees. L'invention concerne enfin des techniques diagnostiques et therapeutiques utiles pour diagnostiquer et pour traiter des maladies, des troubles et/ou des etats associes a ces nouvelles proteines humaines secretees.

4/3,AB/12 (Item 12 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT
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00802240

INHIBITION OF ANGIOGENESIS BY ANTIBODIES AGAINST HIGH MOLECULAR WEIGHT KININOGEN DOMAIN 5

INHIBITION DE L'ANGIOGENESE PAR DES ANTICORPS AVEC DU KININOGENE DE HAUT POIDS MOLECULAIRE DU DOMAINE 5

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200134195 A1 20010517 (WO 0134195) Application: WO 2000US30975

20001110 (PCT/WO US0030975) Priority Application: US 99165165 19991112

Designated States: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR (OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 7135

English Abstract

Antibodies directed against an antigenic determinant of high molecular weight kininogen domain 5, particularly a determinant located in the region formed by light chain amino acids Gly(440) to Lys(502), inhibit angiogenesis.

French Abstract

Selon l'invention, des anticorps sont diriges contre un determinant du kinogene antigenique de haut poids moleculaire du domaine 5, en particulier un determinant situe dans la region formee par des chaine legeres d'acides amines Gly(440) a Lys(502), ce qui permet d'inhiber l'angiogenese.

4/3,AB/13 (Item 13 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT
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00800529

32 HUMAN SECRETED PROTEINS
32 PROTEINES HUMAINES SECRETEES

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French Abstract

L'invention porte sur de nouvelles proteines humaines secretees et sur des acides nucleiques isolés contenant les zones de codage des genes codant pour ces proteines. L'invention porte également sur des procedes diagnostiques et therapeutiques de traitement de maladies, troubles et/ou etats associes a ces nouvelles proteines humaines secretees.

4/3,AB/14 (Item 14 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00783818

DOSAGES FOR TREATMENT WITH ANTI-ErbB2

ANTIBODIES

DOSAGES POUR TRAITEMENT AVEC DES ANTICORPS

ANTI-ErbB2

Patent Applicant/Assignee:

4/3,AB/16 (Item 16 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00771946

A METHOD FOR PREPARING MODIFIED

POLYPEPTIDES

METHODE DE PRODUCTION DE POLYPEPTIDES

MODIFIES

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200104287 A1 20010118 (WO
0104287) Application: WO 2000DK371 20000706
(PCT/WO DK0000371) Priority Application: DK 99988
19990707; DK 991196 19990827; DK 2000339
20000302; DK 2000804 20000518

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI
GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
TZ UA UG UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE (OA) BF BJ CF CG CI CM GA GN GW ML MR
NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 28193

English Abstract

Methods for producing polypeptide with altered immunogenicity or improved stability properties are disclosed. The methods involve a) expressing a diversified population of nucleotide sequences encoding a polypeptide of interest, b) screening the polypeptides expressed in step a) for function, immunogenicity and/or stability, c) selecting functional polypeptides having altered immunogenicity and/or increased stability, e.g. functional in vivo half-life as compared to the polypeptide of interest, and d) optionally subjecting the nucleotide sequence encoding the polypeptide selected in step c) to one or more repeated cycles of steps a)-c). In a further step the expressed polypeptides of step a) or c) can be conjugated to at least one non-polypeptide moiety. French Abstract

L'invention concerne des methodes de production de polypeptides presentant une antigenicite modifiee ou une plus grande stabilite. Ces methodes consistent a) a exprimer une population diversifiee de sequences nucleotidiques codant pour un polypeptide d'interet, b) a cribler les polypeptides exprimes dans l'etape a) pour leur fonction, leur antigenicite et/ou leur stabilite, c) a selectionner les polypeptides fonctionnels presentant une antigenicite modifiee et/ou une plus grande stabilite, par exemple une demi-vie in vivo fonctionnelle par comparaison avec le polypeptide d'interet, et d) a eventuellement soumettre la sequence nucleotidique codant pour le polypeptide selectionne dans l'etape c) a un ou plusieurs cycles repetes comprenant les etapes a)-c). Dans une etape ulterieure, les polypeptides exprimes des etapes a) ou c) peuvent etre conjugues a au moins un fragment non polypeptidique.

4/3,AB/17 (Item 17 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00759536

VASCULAR ENDOTHELIAL GROWTH FACTOR

VARIANTS

VARIANTS DU FACTEUR DE CROISSANCE

ENDOTHELIALE

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Patent and Priority Information (Country, Number, Date):

Patent: WO 200071713 A1 20001130 (WO
0071713) Application: WO 2000US13536
20000518 (PCT/WO US0013536) Priority Application:
US 99135312 19990520

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY CA CH CN CR CU CZ CZ (utility model) DE DE
(utility model) DK DK (utility model) DM DZ EE EE
(utility model) ES FI FI (utility model) GB GD GE GH GM
HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU
SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ
UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE (OA) BF BJ CF CG CI CM GA GN GW ML MR
NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 19920

English Abstract

The invention is directed to a method of enhancing the
biological activity of vascular endothelial growth factors
(*VEGF*). The invention further concerns certain
VEGF variants having enhanced biological activity,
methods and means for preparing these variants, and
pharmaceutical compositions comprising them. In a
further aspect, the invention concerns methods of
treatment using, and articles of manufacture containing
such *VEGF* variants.

French Abstract

L'invention se rapporte a une methode visant a accroitre
l'activite biologique des facteurs de croissance
endotheliale. Elle se rapporte notamment a certains
variants des *VEGF* qui presentent une activite
biologique accrue, a des methodes et unites de
preparation ces variants et a des compositions
pharmaceutiques contenant ces variants. Dans une autre
realisation, l'invention se rapporte a des methodes de
traitement mettant en oeuvre ces variants et a des
produits manufactures les contenant.

4/3,AB/18 (Item 18 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00758405

VASCULAR ENDOTHELIAL GROWTH FACTOR DIMERS
DIMERES, FACTEURS DE CROISSANCE DE
L'ENDOTHELIUM VASCULAIRE Patent

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Newport Beach, CA 92660, US, Patent and Priority
Information (Country, Number, Date):

Patent: WO 200071716 A2-A3 20001130 (WO
0071716) Application: WO 2000US13636
20000518 (PCT/WO US0013636) Priority Application:
US 99135312 19990520; US 2000177407 20000120

Designated States: AE AG AL AM AT AU AZ BA BB BG
BR BY CA CH CN CR CU CZ CZ (utility model) DE DE
(utility model) DK DK (utility model) DM DZ EE EE
(utility model) ES FI FI (utility model) GB GD GE GH GM
HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU
SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ
UA UG US UZ VN YU ZA ZW

(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE (OA) BF BJ CF CG CI CM GA GN GW ML MR
NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW

(EA) AM AZ BY KG KZ MD RU TJ TM

Publication Language: English

Filing Language: English

Fulltext Word Count: 25303

English Abstract

This invention concerns novel vascular endothelial
growth factor (*VEGF*) dimers, compositions containing
such dimers, processes for making such dimers, and
methods for the treatment of various diseases by

administering such dimers or compositions.

French Abstract

L'invention porte sur de nouveaux dimères, facteurs de croissance de l'endothélium vasculaire (*VEGF*), sur des compositions les contenant, sur leurs processus d'obtention, et sur des méthodes de traitement de différentes maladies par administration de ces dimères et de ces compositions.

4/3,AB/19 (Item 19 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00732462
BIOMATERIALS FORMED BY NUCLEOPHILIC
ADDITION REACTION TO CONJUGATED
UNSATURATED GROUPS
BIOMATERIAUX FORMES PAR REACTION
D'ADDITION NUCLEOPHILE A DES GROUPES NON
SATURES CONJUGUES
4/3,AB/20 (Item 20 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00578802
METHODS FOR MAKING PROTEINS CONTAINING
FREE *CYSTEINE* RESIDUES TECHNIQUES
PERMETTANT DE PRODUIRE DES PROTEINES
CONTENANT DES RESIDUS CYSTEINE LIBRES
Patent Applicant/Assignee:
BOLDER BIOTECHNOLOGY INC,
COX George N,
DOHERTY Daniel H,
ROSENDAHL Mary S,
Inventor(s):
COX George N,
DOHERTY Daniel H,
ROSENDAHL Mary S,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200042175 A1 20000720 (WO
0042175) Application: WO 2000US931 20000114
(PCT/WO US0000931) Priority Application: US
99116041 19990114
Designated States: AE AL AM AT AU AZ BA BB BG BR
BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM
HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA
ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY
KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB
GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
GW ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 42386

English Abstract

The present invention relates to novel methods of making soluble proteins having free cysteines in which a host cell is exposed to a cysteine blocking agent. The soluble proteins produced by the methods can then be modified to increase their effectiveness. Such modifications include attaching a PEG moiety to form pegylated proteins.

French Abstract

L'invention concerne des techniques qui permettent de produire des protéines solubles contenant des cystéines libres. Selon lesdites techniques, on expose une cellule hôte à un agent bloquant la cystéine, puis on modifie éventuellement les protéines solubles obtenues afin d'accroître leur efficacité. Ces modifications peuvent consister à fixer un groupe PEG afin de former des protéines pegylées.

4/3,AB/21 (Item 21 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00572732
PROSTACYCLIN-STIMULATING FACTOR-2
FACTEUR-2 STIMULANT DE PROSTACYCLINE
Patent Applicant/Assignee:
HUMAN GENOME SCIENCES INC,
RUBEN Steven M,
YOUNG Paul E,
Inventor(s):
RUBEN Steven M,
YOUNG Paul E,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200036105 A1 20000622 (WO
0036105) Application: WO 99US29945 19991216
(PCT/WO US9929945) Priority Application: US
98113009 19981218
Designated States: AL AM AT AU AZ BA BB BG BR BY
CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM
KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD
RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT
LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR
NE SN TD TG
Publication Language: English
Fulltext Word Count: 98102

English Abstract

The present invention relates to a novel human polypeptide called Prostacyclin-Stimulating Factor-2 (PSF-2), and isolated polynucleotides encoding this polypeptide. Also provided are vectors, host cells, antibodies, and recombinant methods for producing this

human polypeptide. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, preventing, and treating disorders related to this novel human polypeptide.

French Abstract

L'invention concerne un nouveau polypeptide humain appele facteur-2 stimulant de prostacycline (PSF-2), et des polynucleotides isoles codant ce polypeptide. L'invention a egalement trait aux vecteurs, cellules hotes, anticorps et methodes de recombinaison destinees a produire ce polypeptide humain. Elle porte, en outre, sur des methodes diagnostiques et therapeutiques servant a diagnostiquer, prevenir et traiter les troubles lies a ce nouveau polypeptide humain.

4/3,AB/22 (Item 22 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00564062

ANTIBODY-SERUM PROTEIN HYBRIDS
HYBRIDES PROTEIQUES D'ANTICORPS ET DE SERUM

Patent Applicant/Assignee:

CELLTECH THERAPEUTICS LIMITED,
SMITH Bryan John,

Inventor(s):

SMITH Bryan John,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200027435 A1 20000518 (WO 0027435) Application: WO 99GB3747 19991110 (PCT/WO GB9903747) Priority Application: GB 9824632 19981110

Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 13394

English Abstract

Hybrid proteins are described which comprise one or more antigen-binding antibody fragments covalently linked to one or more serum carrier proteins. The hybrid proteins can bind antigens, have a long half-life i(in vivo) and can be used in medicine for therapy and diagnosis.

French Abstract

L'invention concerne des proteines hybrides qui comprennent un ou plusieurs fragments d'anticorps se liant aux antigenes lies par covalence a une ou plusieurs proteines porteuses de serum. Les proteines hybrides

peuvent lier des antigenes, presenter une grande demi-vie i(n vivo) et peuvent etre utilisees en medecine pour des applications therapeutiques et de diagnostic.

4/3,AB/23 (Item 23 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00554839

PLATELET-DERIVED GROWTH FACTOR C, DNA CODING THEREFOR, AND USES THEREOF FACTEUR DE CROISSANCE C DERIVE DES PLAQUETTES, ADN LE CODANT ET SES UTILISATIONS

Patent Applicant/Assignee:

LUDWIG INSTITUTE FOR CANCER RESEARCH,
HELSINKI UNIVERSITY LICENSING LTD,

Inventor(s):

ERIKSSON Ulf,
AASE Karin,
LI Xuri,
PONTEN Annica,
UUTELA Marko,
ALITALO Kari,
OESTMAN Arne,
HELDIN Carl-Henrik,
BETSHOLZ Christer,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200018212 A2 20000406 (WO 0018212) Application: WO 99US22668 19990930 (PCT/WO US9922668) Priority Application: US 98102461 19980930; US 98108109 19981112; US 98110749 19981203; US 98113002 19981218; US 99135426 19990521; US 99144022 19990715

Designated States: AE AU BA BB BG BR CA CN CU CZ EE GD HR HU ID IL IN IS JP KP KR LC LK LR LT LV MG MK MN MX NO NZ PL RO RU SG SI SK SL TR TT UA UZ VN YU GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

Publication Language: English

Fulltext Word Count: 20335

4/3,AB/24 (Item 24 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00524368

TARGETED GENE DELIVERY TO CELLS BY FILAMENTOUS BACTERIOPHAGE ADMINISTRATION DE GENES CIBLES DANS DES CELLULES AU MOYEN DE BACTERIOPHAGES FILAMENTEUX

Patent Applicant/Assignee:

THE REGENTS OF THE UNIVERSITY OF

CALIFORNIA,
MARKS James D,
POUL Marie Alix,
BECERRIL Baltazar,

Inventor(s):

MARKS James D,
POUL Marie Alix,
BECERRIL Baltazar,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9955720 A1 19991104

Application: WO 99US7398 19990423 (PCT/WO
US9907398) Priority Application: US 9882953

19980424; US 99249402 19990212 Designated States:
AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ
DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK
MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS
MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM
AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT
SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD
TG

Publication Language: English

Fulltext Word Count: 30019

English Abstract

This invention provides methods specifically delivering and expressing heterologous nucleic acids in target cells. The methods generally involve providing a phage externally displaying a heterologues targeting protein (e.g., a scFv) and containing a heterologous nucleic acid; and contacting the target cell with the said phage whereby the phage is internalized into the cell and wherein the heterologous nucleic acid is transcribed, and optionally translated, within the cell.

French Abstract

L'invention porte sur des procedes visant a administrer et exprimer specifiquement des acides nucleiques heterologues dans des cellules cibles. Ces procedes consistent generalement a produire un phage presentant exterieurement une proteine de ciblage heterologue (telle que scFv) et contenant un acide nucleique heterologue ; et mettre en contact la cellule cible avec le phage, ce dernier etant internalise dans la cellule, et l'acide nucleique heterologue est transcrit, puis eventuellement traduit, dans la cellule.

4/3,AB/25 (Item 25 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00524015
INTERNALIZING ErbB2 ANTIBODIES
ANTICORPS ERBB2 D'INTERNALISATION

Patent Applicant/Assignee:
THE REGENTS OF THE UNIVERSITY OF
CALIFORNIA,

MARKS James D,
POUL Marie Alix,

Inventor(s):

MARKS James D,
POUL Marie Alix,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9955367 A1 19991104

Application: WO 99US7395 19990423 (PCT/WO
US9907395) Priority Application: US 9882953

19980424; US 99250056 19990212 Designated States:
AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ
DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK
MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS
MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM
AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT
SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD
TG

Publication Language: English

Fulltext Word Count: 29966

English Abstract

This invention provides novel erbB2-binding internalizing antibodies. The antibodies, designated F5 and C1, specifically bind to c-erbB2 antigen and, upon binding, are readily internalized into the cell bearing the c-erbB2 marker. Chimeric molecules comprising the F5 and/or C1 antibodies attached to one or more effector molecules are also provided.

French Abstract

L'invention porte sur de nouveaux anticorps d'internalisation a liaison ERBB2. Les anticorps, appeles F5 et C1, se lient specifiquement a l'antigene c-erbB2 et, lors de la liaison, sont facilement internalises dans la cellule supportant le marqueur c-erbB2. L'invention porte egalement sur des molecules chimeres comprenant les anticorps F5 et/ou C1 lies a une ou plusieurs molecules effectrices.

4/3,AB/26 (Item 26 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00502523
COMPOUNDS AND METHODS FOR MODULATING
SYNAPTIC STABILITY
COMPOSES ET PROCEDES SERVANT A MODULER LA
STABILITE SYNAPTIQUE Patent Applicant/Assignee:
McGILL UNIVERSITY,
BLASCHUK Orest W,
GOUR Barbara J,

Inventor(s):

BLASCHUK Orest W,
GOUR Barbara J,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9933875 A1 19990708

Application: WO 98CA1207 19981223 (PCT/WO

CA9801207) Priority Application: US 97996679

19971223

Designated States: AL AM AT AU AZ BA BB BG BR BY
CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU
ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM
KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ
TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN
TD TG

Publication Language: English

Fulltext Word Count: 20784

English Abstract

Cyclic peptides and compositions comprising such cyclic peptides are provided. The cyclic peptides comprise a cadherin cell adhesion recognition sequence HAV. Methods for using such peptides and compositions for modulating synaptic stability are also provided.

French Abstract

L'invention concerne des peptides cycliques et des compositions contenant ces peptides cycliques. Ces derniers comprennent une sequence HAV de reconnaissance de l'adhesion cellulaire a la cadherine. Elle concerne egalement des procedes permettant de mettre en application ces peptides et ces compositions afin de moduler la stabilite synaptique.

4/3,AB/27 (Item 27 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00484197

PEPTIDE SEQUENCES AS HINGE REGIONS IN
PROTEINS LIKE IMMUNOGLOBULIN FRAGMENTS
AND THEIR USE IN MEDICINE
PEPTIDES

Patent Applicant/Assignee:

CELLTECH THERAPEUTICS LIMITED,
HUMPHREYS David Paul,

Inventor(s):

HUMPHREYS David Paul,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9915549 A2 19990401

Application: WO 98GB2851 19980921 (PCT/WO

GB9802851) Priority Application: GB 9720054 19970919

Designated States: AL AM AT AU AZ BA BB BG BR BY
CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU
ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD

MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM
KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ
TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC
NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN
TD TG

Publication Language: English

Fulltext Word Count: 13485

English Abstract

Peptides of the formula (1) NTCPPCPXYCPPCPAC are described wherein X and Y, which may be the same or different, is each a neutral aliphatic L-amino acid residue, and protected and reactive derivatives thereof. The peptides may be used as hinge regions in proteins, where they are capable of being covalently coupled to achieve dimeric structure, for example as found in antibodies.

French Abstract

La presente invention concerne des peptides representes par la formule (1): NTCPPCPXYCPPCPAC. Dans cette formule, X et Y, qui peuvent etre identiques ou differents, representent un reste d'acide amine L aliphatique neutre et des derives reactifs et proteges de ceux-ci. Ces peptides peuvent etre utilises sous forme de regions charniere dans des proteines dans lesquelles ils peuvent etre couples de maniere covalente de facon a realiser une structure dimere, telle que celle existant dans des anticorps.

4/3,AB/28 (Item 28 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00443453

VASCULAR ENDOTHELIAL GROWTH FACTOR C
(VEGF-C) PROTEIN AND GENE, MUTANTS THEREOF,
AND USES THEREOF
PROTEINE ET GENE DU FACTEUR DE CROISSANCE
VASCULAIRE ENDOTHELIAL C (VEGF-C),
MUTANTS DE CE DERNIER ET UTILISATIONS

Patent Applicant/Assignee:

THE LUDWIG INSTITUTE FOR CANCER RESEARCH,
HELSINKI UNIVERSITY LICENSING LTD OY,
ALITALO Kari,
JOUKOV Vladimir,

Inventor(s):

ALITALO Kari,
JOUKOV Vladimir,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9833917 A1 19980806

Application: WO 98US1973 19980202 (PCT/WO
US9801973) Priority Application: US 97795430
19970205

Designated States: AU CA CN JP NZ US US US US US
US US AT BE CH DE DK ES FI FR GB GR IE IT LU MC
NL PT SE

Publication Language: English

Fulltext Word Count: 53275

English Abstract

Provided are purified and isolated VEGF-C polypeptides capable of binding to at least one of KDR receptor tyrosine kinase (VEGFR-2) and Flt4 receptor tyrosine kinase (VEGFR-3); analogs of such peptides that have VEGF-C-like or VEGF-like biological activities or that are VEGF or VEGF-C inhibitors; polynucleotides encoding the polypeptides; vectors and host cells that embody the polynucleotides; pharmaceutical compositions and diagnostic reagents comprising the polypeptides; and methods of making and using the polypeptides.

French Abstract

Polypeptides VEGF-C purifiés et isolés, capables de se lier à au moins une des tyrosine kinases suivantes: tyrosine kinase à récepteur KDR (VEGFR-2) et tyrosine kinase à récepteur Flt4 (VEGFR-3). L'invention concerne également des analogues de tels peptides, présentant des activités biologiques de type VEGF-C ou VEGF ou qui sont des inhibiteurs de VEGF ou de VEGF-C, ainsi que des polynucleotides codant ces polypeptides, des vecteurs et cellules hôtes qui contiennent ces polynucleotides, des compositions pharmaceutiques et réactifs pour diagnostic contenant ces polypeptides et des procédés pour produire et utiliser ces polypeptides.

4/3,AB/29 (Item 29 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00440930

TISSUE FACTOR METHODS AND COMPOSITIONS
FOR COAGULATION AND TUMOR TREATMENT
METHODES ET COMPOSITIONS DE
THROMBOPLASTINE TISSULAIRE POUR LE
TRAITEMENT DE LA COAGULATION ET DES
TUMEURS

Patent Applicant/Assignee:

BOARD OF REGENTS THE UNIVERSITY OF TEXAS
SYSTEM,

THORPE Philip E,
KING Steven W,
GAO Boning,

Inventor(s):

THORPE Philip E,
KING Steven W,
GAO Boning,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9831394 A2 19980723

Application: WO 98US1012 19980120 (PCT/WO
US9801012) Priority Application: US 9735920
19970122; US 9736205 19970127; US 9742427
19970327

Designated States: AL AM AT AU AZ BA BB BG BR BY
CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU
ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT UA UG US US US UZ VN YU ZW
GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD
RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU
MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN
TD TG

Publication Language: English

Fulltext Word Count: 70089

English Abstract

The invention embodies the surprising discovery that Tissue Factor (TF) compositions and variants thereof specifically localize to the blood vessels within a vascularized tumor following systemic administration. The invention therefore provides methods and compositions comprising coagulant-deficient Tissue Factor for use in effecting specific coagulation and for use in tumor treatment. The TF compositions and methods of present invention may be used alone, as TF conjugates with improved half-life, or in combination with other agents, such as conventional chemotherapeutic drugs, targeted immunotoxins, targeted coaguligands, and/or in combination with Factor VIIa(FVIIa) or FBVIIa activators.

French Abstract

La présente invention a trait à la découverte intéressante de la localisation spécifique de compositions de thromboplastine tissulaire (TF) et de variantes de cette dernière dans les vaisseaux sanguins, à l'intérieur d'une tumeur vascularisée, à la suite d'une administration systémique. L'invention concerne donc des méthodes et compositions comprenant une thromboplastine tissulaire déficiente en coagulants destinée à être utilisée pour effectuer une coagulation spécifique et pour traiter des tumeurs. Les compositions et méthodes de TF de la présente invention peuvent être utilisées seules, comme conjuguées de TF présentant une demi-vie améliorée; ou en combinaison avec d'autres agents, tels que des médicaments chimiothérapeutiques, des immunotoxines ciblées, des coaguligands cibles; et/ou en combinaison avec un Facteur VIIa(FVIIa) ou des activateurs de FVIIa.

4/3,AB/30 (Item 30 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
(c) 2002 WIPO/Univentio. All rts. reserv.

00364924
RECEPTOR LIGAND *VEGF*-C
FACTEUR DE CROISSANCE ENDOTHELIAL
VASCULAIRE (*VEGF*-C) EN TANT QUE LIGAND DE
RECEPTEUR

Patent Applicant/Assignee:

HELSINKI UNIVERSITY LICENSING LTD OY,
ALITALO Kari,
JOUKOV Vladimir,

Inventor(s):

ALITALO Kari,
JOUKOV Vladimir,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9705250 A2 19970213

Application: WO 96FI427 19960801 (PCT/WO

FI9600427) Priority Application: US 95510133

19950801; US 96585895 19960112; US 96601132

19960214; US 96671573 19960628

Designated States: AU CA CN JP NO NZ US AT BE CH

DE DK ES FI FR GB GR IE IT LU MC NL PT SE

Publication Language: English

Fulltext Word Count: 41404

English Abstract

Provided are polypeptide ligands for the receptor tyrosine kinase, Flt4. Also provided are cDNAs and vectors encoding the ligands, pharmaceutical compositions and diagnostic reagents comprising the ligands, and methods of making and using the ligands.

French Abstract

La presente invention se rapporte a des ligands polypeptidiques pour le recepteur tyrosine kinase, Flt4. L'invention decrit egalement des ADN complementaires et des vecteurs codant les ligands, des compositions pharmaceutiques et des reactifs diagnostiques comportant les ligands, ainsi que leurs procedes de fabrication et d'utilisation.

4/3,AB/31 (Item 31 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00233952

VASCULAR PERMEABILITY FACTOR TARGETED
COMPOUNDS

COMPOSES CIBLES SUR LE FACTEUR DE
PERMEABILITE VASCULAIRE

Patent Applicant/Assignee:

BETH ISRAEL HOSPITAL ASSOCIATION,

Inventor(s):

SENGER Donald R,
DVORAK Harold F,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9308210 A1 19930429

Application: WO 92US8816 19921015 (PCT/WO

US9208816) Priority Application: US 91384 19911018

Designated States: AU CA FI JP NO AT BE CH DE DK ES
FR GB GR IE IT LU MC NL SE

Publication Language: English

Fulltext Word Count: 5927

English Abstract

New compounds that bind specifically to vascular permeability factor (VPF) are used in methods of targeting these compounds, which include effector molecules that are, e.g., toxic, radioactive, or serve as marker labels, for tumor cells and the associated blood vessel endothelial cells, based on the discovery that VPF concentrates selectively in the endothelium and basement membrane lining tumor-associated blood vessels to a far greater degree than in normal vessels. By targeting VPF rather than the tumor cells themselves, the invention avoids the problems of tumor heterogeneity and diffusion distance.

French Abstract

De nouveaux composees qui se lient de maniere specifique aux facteurs de permeabilite vasculaire (FPV) sont utilises dans des procedes de ciblage de ces composees, et comprennent des molecules effectrices qui sont par exemple toxiques, radio-actives ou qui servent d'etiquettes de marquage, pour des cellules tumorales et les cellules endotheliales associees de vaisseaux sanguins, l'invention se fonde sur la decouverte que le facteur de permeabilite vasculaire (FPV) se concentre de maniere selective dans les vaisseaux sanguins associes a une tumeur de garniture de membrane de base et de l'endothelium dans une proportion bien plus grande que dans des vaisseaux normaux. En ciblant le facteur de permeabilite vasculaire (FPV) plutot que les cellules tumorales elles-memes, l'invention evite les problemes de la distance de diffusion et de l'heterogeneite des tumeurs.

? ds

Set Items Description

S1 657 (FREE OR EXTRA)()(CYS OR CYSTEINE)
AND (DISULFIDE OR DISULPHIDE)

S2 465 (FREE OR EXTRA)()(CYS OR CYSTEINE)
AND (DISULFIDE OR DISULPHIDE)()BOND?

S3 403 RD (unique items)

S4 31 S3 AND VEGF

? s s3 not s4

403 S3

31 S4

S5 372 S3 NOT S4

? t s4/kwic/all

4/KWIC/1 (Item 1 from file: 349)

DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.

Fulltext Availability:

Detailed Description

4/KWIC/2 (Item 2 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

Detailed Description

4/KWIC/3 (Item 3 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
METHODS FOR REFOLDING PROTEINS
CONTAINING *FREE* *CYSTEINE* RESIDUES
Fulltext Availability:
Detailed Description
Claims

Detailed Description

METHODS FOR REFOLDING PROTEINS
CONTARSTING
FREE *CYSTEINE* RESIDUES

4/KWIC/4 (Item 4 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

4/KWIC/6 (Item 6 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

4/KWIC/7 (Item 7 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description
Claims

4/KWIC/9 (Item 9 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
VEGF-D/*VEGF*-C/*VEGF* PEPTIDOMIMETIC
INHIBITOR INHIBITEUR PEPTIDOMIMETIQUE DE
VEGF-D/*VEGF*-C/*VEGF* Fulltext Availability:
Detailed Description
Claims

4/KWIC/11 (Item 11 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

4/KWIC/12 (Item 12 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

4/KWIC/13 (Item 13 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
4/KWIC/14 (Item 14 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

4/KWIC/15 (Item 15 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description

4/KWIC/17 (Item 17 from file: 349)
DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts.
reserv.
Fulltext Availability:
Detailed Description
Claims

English Abstract

The invention is directed to a method of enhancing the biological activity of vascular endothelial growth factors (*VEGF*). The invention further concerns certain *VEGF* variants having enhanced biological activity, methods and means for preparing these variants, and pharmaceutical compositions comprising them. In a further aspect, the invention concerns methods of treatment using, and articles of manufacture containing such *VEGF* variants.

French Abstract

...invention se rapporte a une methode visant a accroitre l'activite biologique des facteurs de croissance endotheliale. Elle se rapporte notamment a certains variants des *VEGF* qui presentent une activite biologique accrue, a des methodes et unites de preparation ces variants et a des compositions

pharmaceutiques contenant ces variants. Dans une...

Detailed Description

... OF THE INVENTION

1. Field of the Invention

This invention is directed to a method of enhancing the biological activity of vascular endothelial growth factors (*VEGF*). The invention further concerns certain *VEGF* variants having enhanced biological activity. The invention also concerns methods and means for preparing these variants, and pharmaceutical compositions comprising them. The invention further concerns methods of treatment using, and articles of manufacture containing such *VEGF* variants.

IL Description of Backoround and Related Art

Vascular endothelial growth factor (*VEGF*), also referred to as vascular permeability factor (VPF), is a secreted protein generally occurring as a homodimer and having multiple biological functions. The native human *VEGF* monomer occurs as one of five known isoforms, consisting of 121, 145, 165, 189, and 206 amino acid residues in length

4/KWIC/18 (Item 18 from file: 349)

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Fulltext Availability:

Detailed Description

Claims

English Abstract

This invention concerns novel vascular endothelial growth factor (*VEGF*) dimers, compositions containing such dimers, processes for making such dimers, and methods for the treatment of various diseases by administering such dimers or compositions.

French Abstract

L'invention porte sur de nouveaux dimères, facteurs de croissance de l'endothélium vasculaire (*VEGF*), sur des compositions les contenant, sur leurs processus d'obtention, et sur des méthodes de traitement de différentes maladies par administration de ces dimères et

...

4/KWIC/20 (Item 20 from file: 349)

DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts. reserv.

METHODS FOR MAKING PROTEINS CONTAINING *FREE* *CYSTEINE* RESIDUES Fulltext Availability:

Detailed Description

Claims

Detailed Description

METHODS FOR MAKING PROTEINS CONTAINING *FREE* *CYSTEINE* RESIDUES

Field of the Invention

5 The present invention relates generally to methods of making proteins and more specifically to recombinant proteins containing a "free" cysteine residue that does not form a *disulfide* *bond*.

Background of the Invention

There is considerable interest on the part of patients and healthcare providers in the development of low cost, long-acting...reactive groups (e.g., imide, vinylsulfone) and different size PEGs (2-40 kDa) are commercially available. At neutral pH, these PEG reagents selectively attach to "*free*" *cysteine* residues, i.e., cysteine residues not involved in *disulfide* *bonds*. Cysteine residues in most proteins participate in *disulfide* *bonds* and are not available for PEGylation using cysteine-reactive PEGs.

Through in vitro mutagenesis using recombinant DNA techniques, additional cysteine residues can be introduced anywhere...

...bond may be deleted or substituted with another amino acid, leaving a native cysteine (the cysteine residue in the protein that normally would form a *disulfide* *bond* with the deleted or substituted cysteine residue) free and available for chemical modification. Preferably the amino acid substituted for the cysteine would be a neutral ...

...four cysteines would be reasonable targets for deletion or substitution by another amino acid.

Several naturally-occurring proteins are known to contain one or more " *free*" *cysteine* residues. Examples of such naturally-occurring proteins include human Interleukin (IL)-2, beta interferon (Mark et al., 1984), G-CSF (Lu et al., 1989) and...

...contain an odd number of cysteine residues, whereas basic fibroblast growth factor contains an even number of cysteine residues. However, expression of recombinant proteins containing *free* *cysteine* residues has been problematic due to reactivity of the free sulfhydryl at physiological conditions. Several recombinant proteins containing free cysteines have been expressed as intracellular...

...2 (Nolark et al., 1985) and beta interferon (DeChiara et al., 1986) have been obtained by substituting another amino acid, e.g., serine, for the *free* *cysteine* residue. It would be preferable to express the recombinant proteins in a soluble, biologically active form to eliminate these extra steps.

One known method of...ompA) signal sequence and the start of the mature hGH protein. While the periplasmic space is believed to be an oxidizing environment that should promote *disulfide* *bond* formation,

coexpression of protein disulfide isomerase with bovine pancreatic trypsin inhibitor resulted in a six-fold increase in the yield of correctly folded protein from...

...The released hGH protein is then purified by column chromatography ((Hsiung et al., 1986).

When similar procedures were attempted to secrete hGH variants containing a *free* *cysteine* residue (five cysteines; 2N+1), it was discovered that the recombinant hGH variants formed multimers and aggregates when isolated using standard osmotic shock and purification...

...the osmotic shock lysates or during purification of the proteins by column chromatography.

Alpha interferon (IFN- α 2) also contains four cysteine residues that form two *disulfide* *bonds*.

IFN- α 2 can be secreted into the E. coli periplasm using the still signal sequence (Voss et al., 1994).

The secreted protein is soluble and...

...recombinant IFN- α 2 can be purified by column chromatography (Voss et al., 1994).

When similar procedures were attempted to secrete IFN- α 2 variants containing a *free* *cysteine* residue (five cysteines- 2N+1), it was discovered that the recombinant IFN- α 2 variants 15 formed multimers and aggregates when isolated using standard purification...
...monomeric IFN- α 2 variant proteins could be purified using column chromatography procedures developed for IFN- α 2.

An alternative method to synthesizing a protein containing a *free* *cysteine* residue is to introduce a thiol group into a protein post-translationally via a chemical reaction with succinimidyl 613 pyridyldithio)propionan-dolhexanoate (LC-SPDP, commercially...

...of long acting recombinant proteins by enhancement of protein molecular weight. A need also for methods that allow secretion and recovery of recombinant proteins containing *free* *cysteine* residues in high yield. The present invention satisfies these needs and provides related advantages as well.

Summary of the Invention

The present invention relates to methods for obtaining a soluble protein having a *free* *cysteine*. The methods are generally accomplished by obtaining a host cell capable of expressing the soluble protein, exposing the host cell to a cysteine blocking agent...attaching a PEG moiety to the soluble protein to form pegylated proteins

in which the PEG moiety is attached to the soluble protein through the *free* *cysteine*. Higher order multimeric proteins involving the coupling of two or more of the soluble proteins are also within the present invention.

The present invention further...

...which two separate fragments are amplified from a target DNA segment.

Description of the Invention

The present invention provides novel methods of obtaining proteins having *free* *cysteine* residues. The invention further provides novel proteins, particularly recombinant proteins, produced by these novel methods as well as derivatives of such recombinant proteins. The novel methods for preparing such proteins are generally accomplished by.

(a) obtaining a host cell capable of expressing a protein having a *free*

4/KWIC/21 (Item 21 from file: 349)

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Fulltext Availability:

Detailed Description

4/KWIC/23 (Item 23 from file: 349)

DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts. reserv.

Fulltext Availability:

Detailed Description

Claims

Detailed Description

... to act primarily via

endothelial receptor tyrosine kinases (RTKs).

Nine different proteins have been identified in the PDGF family, namely two PDGFs (A and B), *VEGF* and six members that are closely related to *VEGF*. The six members closely related to *VEGF* are: *VEGF*-B, described in International Patent Application PCT/US96/02957 (WO 96/26736) and in U.S. Patents 5,840,693 and 5,607,918 by Ludwig Institute for Cancer Research and The University of Helsinki; *VEGF*-C, described in Joukov et al., EMBO J., 1996 15 290-298 and Lee et al., Proc.

Natl. Acad. Sci. USA, 1996 93 1988-1992; *VEGF*-D, described in International Patent Application No. PCT/US97/14696 (WO

98/07832), and Achen et al., Proc. Natl. Acad. Sci. USA, 1998 95 548...

...by Human Genome Sciences, Inc;

and VEGF3, described in International Patent Application No.

PCT/US95/07283 (WO 96/39421) by Human Genome Sciences, Inc.

Each *VEGF* family member has between 30% and 45% amino acid sequence identity with *VEGF*. The *VEGF* family members share a *VEGF* homology domain which contains the six cysteine residues which form the cysteine knot motif. Functional

characteristics of the *VEGF* family include varying degrees of mitogenicity for endothelial cells, induction of vascular permeability and angiogenic and lymphangiogenic properties.

Vascular endothelial growth factor (*VEGF*) is a homodimeric glycoprotein that has been isolated from several sources. *VEGF* shows highly specific mitogenic activity for endothelial cells. *VEGF* has important regulatory functions in the formation of new blood vessels during embryonic

vasculogenesis and in angiogenesis during adult life (Carmeliet et al., Nature, 1996...

...al.,

Nature, 1996 380 439-442; reviewed in Ferrara and Davis-Smyth,, Endocrine Rev., 1997 18

4/KWIC/31 (Item 31 from file: 349)

DIALOG(R)File 349:(c) 2002 WIPO/Univentio. All rts. reserv.

Fulltext Availability:

Detailed Description

Detailed Description

... the

isolation of VPF and the creation of antibodies against VPF_e

VPF is now known to be the same molecule as vascular endothelial growth factor (*VEGF*), as evidenced by the following points of identity: (1) molecular

weight and NH₂ - terminal amino acid sequence of the purified proteins (Ferrara, N., et al...

...IA (1989)), and (3) probably identical biological activities (Connolly, D.T., et al., J. Clin. Invest., 84: 1470-1478 (1989))e

Alternative forms of VPF/*VEGF* have been identified, and it has been determined that these forms arise as a consequence of alternative mRNA splicing of transcripts from the VPF/*VEGF* gene. Tischer,, E., et al., LT. Biol. Chem., 266: 11947-11954 (1991)e As used herein,, IIVPFII encompasses all such alternative forms.

Summary of the...be produced separately and later coupled by means of a non-peptide covalent bond.

For example, the covalent linkage may take the form of a *disulfide* *bond*. In this case, the DNA

encoding this antibody can be engineered, by conventional methods, to contain an *extra* *cysteine* codon. The cysteine should be positioned so as to not interfere with the VPF binding activity of the compound.

For a *disulfide* *bond* linkage, the toxin molecule is also derivatized with a sulfhydryl group reactive with the cysteine of the modified antibody. In the case of a peptide antibody are purified, both sulfur groups are reduced,, cytotoxin and antibody are mixed (in a ratio of about 1:5 to 1:20). and *disulfide* *bond* formation is allowed to proceed to completion (generally 20 to 30 minutes) at

room temperature. The mixture is then dialyzed against phosphate buffered saline to...

? ds

Set Items Description

S1 657 (FREE OR EXTRA)()(CYS OR CYSTEINE) AND (DISULFIDE OR DISULPHIDE)

S2 465 (FREE OR EXTRA)()(CYS OR CYSTEINE) AND (DISULFIDE OR DISULPHIDE)()BOND?

S3 403 RD (unique items)

S4 31 S3 AND VEGF

S5 372 S3 NOT S4

? s s5 not (free or extra)()(cys or cysteine)()codon

372 S5

1223481 FREE

141487 EXTRA

40410 CYS

125381 CYSTEINE

79341 CODON

11 (FREE OR EXTRA)(W)(CYS OR CYSTEINE)(W)CODON S6 362 S5 NOT (FREE OR EXTRA)()(CYS OR CYSTEINE)()CODON ? s s6 and (cys or cysteine)(5n)(disulfide or disulphide)

362 S6

40410 CYS

125381 CYSTEINE

72618 DISULFIDE

11101 DISULPHIDE

7362 (CYS OR CYSTEINE)(5N)(DISULFIDE OR DISULPHIDE) S7 208 S6 AND (CYS OR CYSTEINE)(5N)(DISULFIDE OR DISULPHIDE) ? +

s7/ti/all

? + s7/3,ab/10, 13, 67, 90, 101, 108

7/3,AB/10 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10455921 99448381 PMID: 10518936

Strong hydrophobic nature of cysteine residues in proteins. Nagano N; Ota M; Nishikawa K

National Institute of Genetics, Shizuoka, Japan.

FEBS letters (NETHERLANDS) Sep 10 1999, 458

(1) p69-71, ISSN 0014-5793 Journal Code: 0155157

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The differences between *disulfide*-*bonding* cystine (*Cys* SS) and *free* *cysteine* (Cys SH) residues were examined by analyzing the statistical distribution of both types of residue in proteins of known structure. Surprisingly, Cys SH residues display stronger hydrophobicity than Cys SS residues. A detailed survey of atoms which come into contact with the sulfhydryl group (sulfur atom) of Cys SH revealed those atoms are essentially the same in number and variety as those of the methyl group of isoleucine, but are quite different to those of the hydroxyl group of serine. Moreover, the relationships among amino acids were also determined using the 3D-profile table of known protein structures. Cys SH was located in the hydrophobic cluster, along with residues such as Met, Trp and Tyr, and was clearly separated from Ser and Thr in the polar cluster. These results imply that free cysteines behave as strongly hydrophobic, and not hydrophilic, residues in proteins

7/3,AB/13 (Item 13 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

09776989 98208581 PMID: 9539778

Activating mutations in the extracellular domain of the fibroblast growth factor receptor 2 function by disruption of the *disulfide* *bond* in the third immunoglobulin-like domain.

Robertson S C; Meyer A N; Hart K C; Galvin B D; Webster M K; Donoghue D J Department of Chemistry and Biochemistry, Center for Molecular Genetics, University of California at San Diego, La Jolla, CA 92093-0367. Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Apr 14 1998, 95 (8) p4567-72, ISSN 0027-8424 Journal Code: 7505876

Contract/Grant No.: DE 12581; DE: NIDCR; GM 07313; GM: NIGMS Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Multiple human skeletal and craniosynostosis disorders, including Crouzon, Pfeiffer, Jackson-Weiss, and Apert syndromes, result from numerous point mutations in the extracellular region of fibroblast growth factor receptor 2 (FGFR2). Many of these mutations create a *free* *cysteine* residue that potentially leads to abnormal *disulfide* *bond* formation and receptor activation; however, for noncysteine mutations, the mechanism of receptor activation remains unclear. We examined the effect of

two of these mutations, W290G and T341P, on receptor dimerization and activation. These mutations resulted in cellular transformation when expressed as FGFR2/Neu chimeric receptors. Additionally, in full-length FGFR2, the mutations induced receptor dimerization and elevated levels of tyrosine kinase activity. Interestingly, transformation by the chimeric receptors, dimerization, and enhanced kinase activity were all abolished if either the W290G or the T341P mutation was expressed in conjunction with mutations that eliminate the *disulfide* *bond* in the third immunoglobulin-like domain (Ig-3). These results demonstrate a requirement for the Ig-3 cysteine residues in the activation of FGFR2 by noncysteine mutations. Molecular modeling also reveals that noncysteine mutations may activate FGFR2 by altering the conformation of the Ig-3 domain near the *disulfide* *bond*, preventing the formation of an intramolecular bond. This allows the unbonded *cysteine* residues to participate in intermolecular *disulfide* *bonding*, resulting in constitutive activation of the receptor.

7/3,AB/67 (Item 31 from file: 349)

DIALOG(R)File 349:PCT FULLTEXT

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00540679

SOLUBLE DERIVATIVES OF ANTI-ANGIOGENIC PEPTIDES

DERIVES DE POLYPEPTIDES

Patent Applicant/Assignee:

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SMITH Richard Anthony Godwin,
BRIGHT Jeremy Richard,
STEWARD Michael,
COX Vivienne Frances,

Inventor(s):

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STEWARD Michael,
COX Vivienne Frances,

Patent and Priority Information (Country, Number, Date):

Patent: WO 200004052 A2 20000127 (WO 0004052) Application: WO 99GB2292 19990716 (PCT/WO GB9902292) Priority Application: GB 9815505 19980716

Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW

ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 11662

English Abstract

It has been found that derivatives of angiogenesis inhibiting proteins may be prepared in which a negative feedback process can be enhanced for therapeutic purposes and which can be targeted to cell membranes and sites of active angiogenesis particularly those of the vascular endothelium. The invention provides a soluble derivative of a polypeptide capable of inhibiting angiogenesis, said derivative comprising a combination of heterologous membrane binding elements covalently associated with the polypeptide so that the derivative acquires affinity for the surface of the vascular endothelium particularly that of growing blood vessels. The soluble polypeptide may be selected from the non-catalytic regions of human plasminogen (within the N-terminal 560 residues of that protein); fragments thereof, particularly those generated by metalloprotease digestion of plasminogen; fragments of related proteins containing kringle domains such as hepatocyte growth factor or apolipoprotein (a), prothrombin, tissue-type plasminogen activator, urinary-type plasminogen activator and hybrids thereof with plasminogen sequences; mutants of the above kringle domains, those containing positively charged to neutral or negatively charged mutations at positions 20, 21, 78 and 79; fragments of collagen, particularly collagen XVIII; fragments of prolactin, the 16kDa N-terminal region of prolactin; neutralising antibodies against receptors for angiogenic mediators; antagonists of integrins involved in angiogenesis; and hybrids, derivatives or muteins thereof. Each membrane binding element with low membrane affinity may have a dissociation constant of 1µM-1mM, and the derivative may incorporate sufficient elements with low affinities for membrane components to result in a 0.01 - 10nM dissociation constant affinity for specific membranes.

French Abstract

On a decouvert que l'on peut preparer des derives des proteines inhibant l'angiogenese dans lesquels un processus de retroaction negative peut etre renforce a des fins therapeutiques et qui peuvent etre diriges sur des membranes de cellules et des sites d'angiogenese active, en particulier sur ceux de l'endothelium vasculaire. L'invention concerne un derive de polypeptide soluble capable d'inhiber l'angiogenese, ledit derive comprenant une combinaison d'elements heterologues liant la membrane, associes par covalence avec le polypeptide de maniere a conferer au derive une affinite pour la surface d'endothelium vasculaire, notamment de celui des vaisseaux sanguins en croissance. Le polypeptide soluble peut etre selectionne depuis des regions non

catalytiques du plasminogene humain (a l'interieur des 560 residus N-terminaux de cette proteine); de ses fragments, notamment de ceux generes par digestion metalloprotease du plasminogene; des fragments des proteines correspondantes contenant des domaines kringle tels que facteur de croissance d'hepatocytes ou apolipoproteine (a), prothrombine, activateur de plasminogene du type tissu, activateur de plasminogene du type urinaire et leurs hybrides avec des sequences plasminogenes; des mutants des domaines kringle mentionnes ci-dessus, de ceux contenant des mutations dans des positions 20, 21, 78 et 79 a charge positive a neutre ou a charge negative; des fragments de collagene, en particulier du collagene XVIII; des fragments de prolactine, de la region N-terminal 16 kDa de la prolactine; des anticorps neutralisants diriges contre les recepteurs pour mediateurs angiogeniques; des antagonistes d'integrines participant a l'angiogenese; et de leurs hybrides, derives ou muteines. Chaque element liant la membrane avec une affinite peu elevee pour les membranes peut avoir une constante de dissociation comprise entre 1µM et 1 mM, le derive pouvant integrer suffisamment d'elements avec des affinites peu elevees pour les composants de membrane pour arriver a une affinite constante de dissociation pour des membranes specifiques comprise entre 0,01 et 10 nM.

7/3,AB/90 (Item 54 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00397380
METHODS FOR PRODUCING SOLUBLE,
BIOLOGICALLY-ACTIVE *DISULFIDE*
BOND-CONTAINING EUKARYOTIC PROTEINS IN
BACTERIAL CELLS PROCEDES DE PRODUCTION DE
PROTEINES EUKARYOTES, SOLUBLES, ACTIVES SUR
PLAN BIOLOGIQUE ET CONTENANT DES
LIAISONS DISULFURE, A L'INTERIEUR DE
CELLULES BACTERIENNES
Patent Applicant/Assignee:
BOARD OF REGENTS THE UNIVERSITY OF TEXAS
SYSTEM,
Inventor(s):
GEORGIOU George,
OSTERMEIER Marc,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9738123 A1 19971016
Application: WO 97US5636 19970404 (PCT/WO
US9705636) Priority Application: US 9614950
19960405
Designated States: AL AM AT AU AZ BA BB BG BR BY
CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN
MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM

TR TT UA UG UZ VN YU GH KE LS MW SD SZ UG AM
AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR
GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA
GN ML MR NE SN TD TG Publication Language: English
Fulltext Word Count: 37312

English Abstract

Disclosed are methods of producing eukaryotic
disulfide *bond* -containing polypeptides in bacterial
hosts, and compositions resulting therefrom.
Co-expression of a eukaryotic foldase and a *disulfide*
bond-containing polypeptide in a bacterial host cell is
demonstrated. In particular embodiments, the methods
have been used to produce mammalian pancreatic trypsin
inhibitor and tissue plasminogen activator (tPA) in
soluble, biologically-active forms, which are isolatable
from the bacterial periplasm. Also disclosed are
expression systems, recombinant vectors, and
transformed host cells.

French Abstract

Cette invention concerne des procedes de production de
polypeptides eucaryotes, solubles, qui sont actifs sur
plan biologique et qui contiennent des liaisons disulfure,
ceci a l'interieur d'hotes bacteriens. Cette invention, qui
concerne egalement les compositions ainsi obtenues, a
permis de demontrer la co-expression d'une foldase
eucaryote et d'un polypeptide contenant une liaison
disulfure a l'interieur d'une cellule bacterienne hote.
Dans des modes de realisation particuliers, ces procedes
ont permis de produire un inhibiteur de trypsine
pancreatique chez les mammiferes ainsi qu'un activateur
plasminogene de tissus (tPA), lesquels se presentent sous
des formes solubles, actives sur le plan biologique, et
pouvant etre isolees du periplasme bacterien. Cette
invention concerne enfin des systemes d'expression, des
vecteurs recombinants, ainsi que des cellules hotes
transformees.

7/3,AB/101 (Item 65 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00308047
COVALENT DIMERS OF KIT LIGAND AND FLT-3/FLK-2
LIGAND
DIMERES COVALENTS DE KIT LIGAND ET DE LIGAND
DE FLT-3/FLK-2 Patent Applicant/Assignee:

CYTOMED INC,
NOCKA Karl H,
LOBELL Robert B,

Inventor(s):

NOCKA Karl H,
LOBELL Robert B,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9526199 A1 19951005

Application: WO 95US3866 19950328 (PCT/WO
US9503866) Priority Application: US 94220379
19940328

Designated States: AM AT AU BB BG BR BY CA CH CN
CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK
LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO
RU SD SE SG SI SK TJ TM TT UA UG US UZ VN KE
MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU
MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN
TD TG Publication Language: English
Fulltext Word Count: 28764

English Abstract

A modified form of KL, the ligand for the c-kit
proto-oncogene, has been prepared wherein the protein
is stabilized by an intermolecular covalent linkage. The
protein can be prepared by expression of a recombinant
protein which is dissolved in denaturant and refolded under
conditions resulting in a disulfide linked dimer. Examples
demonstrate the purification and characterization of
this *disulfide*-linked *cysteine* dimer kit ligand
(KL-CD) which contains at least one intermolecular
disulfide *bond* and has at least ten-fold greater
activity in promoting cell proliferation than native,
non-covalently linked KL, as measured in in vitro assays.
The figure shows the proliferative activity of murine
KL-NC, murine KL-CD, murine KL-Ig fusion, and human
KL-Ig fusion on an MO7e cell line.

French Abstract

L'invention concerne une forme modifiee de KL, ligand
pour le proto-oncogene c-kit, dans laquelle la proteine
est stabilisee par une liaison de covalence
intermoleculaire. La proteine peut etre preparee par
expression d'une proteine recombinnee, dissoute dans un
agent denaturant et repliee dans des conditions
permettant de parvenir a un dimere lie a un disulfure.
Des exemples illustrent la purification et la
caracterisation de ce kit ligand de dimere de cysteine lie
a un disulfure (KL-CD) contenant au moins un pont
disulfure intermoleculaire et presentant une activite
favorisant la proliferation cellulaire au moins dix fois
superieure a celle des KL natifs, non lies par covalence,
comme l'ont montre les mesures effectuees dans les
techniques in vitro. La figure 9 presente l'activite
proliferative du KL-NC murin, du KL-CD murin, de la
fusion de KL-Ig murin et de la fusion de KL-Ig humain sur
une lignee cellulaire MO7e.

7/3,AB/108 (Item 72 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00274314
CONJUGATES OF PROTEINS AND BIFUNCTIONAL
LIGANDS
CONJUGUES DE PROTEINES ET DE LIGANDS A

DOUBLE FONCTION

Patent Applicant/Assignee:

IMMUNOMEDICS INC,

Inventor(s):

GRIFFITHS Gary L,

DIRIL Habibe,

HANSEN Hans J,

Patent and Priority Information (Country, Number, Date):

Patent: WO 9422490 A1 19941013

Application: WO 94US2968 19940325 (PCT/WO

US9402968) Priority Application: US 9338416

19930329

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DK ES FI GB HU JP KP KR KZ LK LU LV MG MN MW NL

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DK ES FR GB GR IE IT LU MC NL PT SE

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English Abstract

Provided are conjugates useful in cancer, cardiovascular or infectious disease detection and/or therapy. The conjugate is of a ligand and protein. The ligand has a moiety capable of binding to mercapto groups and is capable of chelating a metal useful for detection or therapy. The protein reacts with a substance associated with a targeted cell, pathologic lesion or pathogen. The protein prior to conjugation has at least one mercapto group which becomes a site for conjugation to the ligand. Also provided are metal chelates of the conjugate, methods of detection and therapy, methods for producing the conjugate and pharmaceutical compositions of the conjugates.

French Abstract

L'invention concerne des conjugues utiles pour la detection et/ou la therapie du cancer, des maladies cardio-vasculaires ou infectieuses. Le conjugué se compose d'un ligand et d'une proteine. Le ligand possede une fraction qui peut se lier aux groupes mercapto et qui peut susciter la chelation d'un metal utile a la detection ou a la therapie. La proteine reagit avec une substance associee a une cellule-cible, une lesion pathologique ou un pathogene. Avant conjugaison, la proteine comporte au moins un groupe mercapto qui devient le site de conjugaison avec le ligand. L'invention concerne egalement des chelates metalliques du conjugué, des procedes de detection et des protocoles therapeutiques, des procedes de production du conjugué et des compositions pharmaceutiques des conjugues.

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\$0.00 36 Type(s) in Format 6 (UDF)

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\$35.32 7.435 DialUnits File349

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\$1.60 1 Type(s) in Format 3 (UDF)

\$185.30 34 Type(s) in Format 5 (UDF)

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\$186.90 172 Types

\$222.22 Estimated cost File349

\$2.11 0.377 DialUnits File5

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\$0.00 18 Types

\$2.11 Estimated cost File5

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\$0.00 42 Types

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\$0.00 6 Type(s) in Format 6 (UDF)

\$0.00 6 Types

\$0.45 Estimated cost File35

OneSearch, 5 files, 8.854 DialUnits FileOS

\$3.46 TELNET

\$232.34 Estimated cost this search

\$302.69 Estimated total session cost 20.710 DialUnits

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